Inflammatory Bowel disease

0034913

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NEWS 48 Feb 26 PCTFULL now contains images
NEWS 49 Mar 04 SDI PACKAGE for monthly delivery of multifile SDI results

NEWS EXPRESS January 6 CURRENT WINDOWS VERSION IS V6.01a,
CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
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0034913

FILE COVERS 1907 - 6 Mar 2003 VOL 138 ISS 10
FILE LAST UPDATED: 5 Mar 2003 (20030305/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s ep0927721/pn
L1 1 EP0927721/PN
(EP927721/PN)

=> d l1 ibib hitstr abs

L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:404974 CAPLUS
DOCUMENT NUMBER: 131:59020
TITLE: Preparation of vitamin D derivatives with phosphorous atoms in the side chains
INVENTOR(S): Steinmeyer, Andreas; Neef, Gunter; Kirsch, Gerald; Schwarz, Katica; Wiesinger, Herbert; Haberey, Martin; Fahnrich, Marianne; Langer, Gernot
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9931112	A1	19990624	WO 1998-EP8137	19981216
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 927721	A1	19990707	EP 1997-250374	19971217 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
DE 19758119	C1	19990729	DE 1997-19758119	19971217
AU 9924134	A1	19990705	AU 1999-24134	19981216
EP 1042335	A1	20001011	EP 1998-966616	19981216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002508383	T2	20020319	JP 2000-539035	19981216

PRIORITY APPLN. INFO.: DE 1997-19758119 A 19971217
EP 1997-250374 A 19971217
WO 1998-EP8137 W 19981216
OTHER SOURCE(S): MARPAT 131:59020
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

0034913

AB The invention relates to novel vitamin D derivs. I [Y1 = H, OH, F, Cl, Br, O2CR5; Y2 = H, COR6; Y2O = .alpha.- or .beta.- bond; R1, R2 = H; R1R2 = CH2; R3, R4 = H, Cl, F, C1-4-alkyl; R3R4 = CH2; R3R4-C(20) = satd. or unsatd. C3-7-cycloalkyl; R5, R6 = C1-12-alkyl, aryl; VW = bond; V = W = OH; V = OH, W = H; X1, X2 = H, OH, OR7, O2CR7, PO(OR8)2, PO(NR82)2, PO(R8)2, OPO(OR8)2, OPO(NR82)2, OPO(R8)2, CH2PO(OR8)2, CH2PO(NR82)2, CH2PO(R8)2; R7 = C1-12-alkyl, aryl; R8 = H, C1-12-alkyl, aryl;; X1X2 = O; n = 0, 1; E1 = PO(OR9)2, PO(NR92)2, PO(R9)2, CO2R9; R9 = H, C1-12-alkyl, aryl; E2 = PO(OR9)2, PO(NR92)2, PO(R9)2, CO2R9, F, Cl, Br, H, C1-12-alkyl, aryl; Q = H, C1-12-alkyl, aryl, OH, O2CR10, F, Cl, Br, NH2, NHR10, N(R10)2; R10 = C1-12-alkyl, aryl; X1E2 = bond, X2 = H, OZ; Z = C1-12-alkyl, aryl, C1-12-acyl, aroyl, E2; X1X2E2Q = triple bond], a method for their prodn., intermediate products of the method as well as their use in producing medicaments. Thus, vitamin D analog II was prepd. from aldehyde III (TBDMS = SiMe2CMe3), via photochem. E/Z-isomerization, Horner-Emmons reaction with (MeO)2P(O)CH2CO2Me, condensation of unsatd. ester IV with MeP(O)(OMe)2 and desilylation with Dowex ion-exchange resin. II has an affinity for calcitriol receptors (competition factor = 10) and shows differentiation induction for HL-60 cells [DR50 = 22] and hypercalcemia induction [DR50 = >>100].
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>
=> s vitamin D
152450 VITAMIN
1956515 D
L2 20659 VITAMIN D
(VITAMIN(W)D)

=> s l2 and inflammatory bowel disease
100292 INFLAMMATORY
9855 BOWEL
582905 DISEASE
3110 INFLAMMATORY BOWEL DISEASE
(INFLAMMATORY(W)BOWEL(W)DISEASE)
L3 18 L2 AND INFLAMMATORY BOWEL DISEASE

=> s vitamin D3
152450 VITAMIN
31725 D3
L4 8790 VITAMIN D3
(VITAMIN(W)D3)

=> s l4 and inflammatory bowel disease
100292 INFLAMMATORY
9855 BOWEL
582905 DISEASE
3110 INFLAMMATORY BOWEL DISEASE
(INFLAMMATORY(W)BOWEL(W)DISEASE)
L5 4 L4 AND INFLAMMATORY BOWEL DISEASE

=> d l5 ibib hitstr abs

L5 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:314727 CAPLUS
DOCUMENT NUMBER: 136:339498

0034913

TITLE: Methods for treating IL-18 mediated disorders
INVENTOR(S): Sims, John E.; Mohler, Kendall M.; Born, Teresa L.
PATENT ASSIGNEE(S): Immunex Corporation, USA
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032374	A2	20020425	WO 2001-US32460	20011017
WO 2002032374	A3	20020919		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002098185	A1	20020725	US 2002-981421	20020118

PRIORITY APPLN. INFO.: US 2000-241408P P 20001018
AB The invention pertains to methods for treating medical disorders characterized by elevated levels or abnormal expression of IL-18 by administering an IL-18 antagonist, such as sol. IL-18 receptor, a sol. IL-18 binding protein and/or an antibody.

=> d his

(FILE 'HOME' ENTERED AT 12:10:14 ON 06 MAR 2003)

FILE 'CAPLUS' ENTERED AT 12:10:26 ON 06 MAR 2003
L1 1 S EP0927721/PN
L2 20659 S VITAMIN D
L3 18 S L2 AND INFLAMMATORY BOWEL DISEASE
L4 8790 S VITAMIN D3
L5 4 S L4 AND INFLAMMATORY BOWEL DISEASE

=> d l5 2-4 ibib hitstr abs

L5 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:147266 CAPLUS
DOCUMENT NUMBER: 134:364800
TITLE: Receptor polymorphisms and diseases
AUTHOR(S): Csaszar, A.; Abel, T.
CORPORATE SOURCE: Faculty of Health Sciences, Department of Medicine and Geriatrics, Semmelweis University, Budapest, H-1135, Hung.
SOURCE: European Journal of Pharmacology (2001), 414(1), 9-22
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with many refs. The aim of our review is to summarize common genetic variations of some receptors assocd. with clin. consequences,

which were not outlined in the previous special issue of this journal. Because of the multiple pathomechanisms of diseases, a set of genetic variation can play a role in the development of pathol. conditions. From the data available three articles would merit a greater interest. In systemic lupus erythematosus the assocns. related to some polymorphisms of Fc-, tumor necrosis factor (TNF) .alpha.- and interferon receptor may explore new autoimmunol. and inflammatory pathomechanisms. In the endocrinol., the androgen receptor repeat polymorphism will exert significant aspects in the development of prostate cancer. The pleiotropic responsibility of **vitamin D3** receptor polymorphism in the pathogenesis of immunol. disorders (primary biliary cirrhosis, **inflammatory bowel disease**, type 1 diabetes mellitus) and of malignancies (malignant melanoma, breast cancer) shed light on the importance of common nuclear receptors. Nevertheless, in the future studies a more consistent approach minimizing requirement bias in the selection of patients will approve our understanding the role of genetic influence on the pathogenesis of diseases.

REFERENCE COUNT: 84 THERE ARE 84 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:588387 CAPLUS
DOCUMENT NUMBER: 134:84446
TITLE: Vitamin D receptor gene polymorphism: association with Crohn's disease susceptibility
AUTHOR(S): Simmons, J. D.; Mullighan, C.; Welsh, K. I.; Jewell, D. P.
CORPORATE SOURCE: Gastroenterology Unit, Radcliffe Infirmary, University of Oxford, Oxford, OX2 6HE, UK
SOURCE: Gut (2000), 47(2), 211-214
CODEN: GUTTAK; ISSN: 0017-5749
PUBLISHER: BMJ Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The vitamin D receptor (VDR) gene represents a strong positional candidate susceptibility gene for **inflammatory bowel disease** (IBD). The VDR gene maps to a region on chromosome 12 that has been shown to be linked to IBD by genome screening techniques. It is the cellular receptor for 1,25(OH)2 **vitamin D3** (calcitriol) which has a wide range of different regulatory effects on the immune system. IBD is characterized by activation of the mucosal immune system. The assocn. of polymorphisms in the VDR gene with susceptibility to IBD were studied. The subjects were European Caucasoids158 patients with ulcerative colitis, 245 with Crohn's disease, and 164 cadaveric renal allograft donor controls. Single nucleotide polymorphisms (TaqI, ApaI, and FokI) in VDR were typed in patients with Crohn's disease, ulcerative colitis, and controls by polymerase chain reaction with sequence specific primers. There were significantly more homozygotes for the TaqI polymorphism at codon 352 of exon 8 (genotype "tt") among patients with Crohn's disease (frequency 0.22) than patients with ulcerative colitis (0.12) or controls (0.12) (odds ratio 1.99; 95% confidence interval 1.14-3.47; p=0.017). This study provides preliminary evidence for a genetic assocn. between Crohn's disease susceptibility and a gene that lies within one of the candidate regions detd. by linkage anal.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS

0034913

ACCESSION NUMBER: 2000:246169 CAPLUS
DOCUMENT NUMBER: 132:260649
TITLE: Increase of bone mineral density with sodium fluoride in patients with Crohn's disease
AUTHOR(S): Von Tirpitz, Christian; Klaus, Jochen; Bruckel, Joachim; Rieber, Andrea; Scholer, Andre; Adler, Guido; Bohm, Bernhard O.; Reinshagen, Max
CORPORATE SOURCE: Department of Medicine, University of Ulm, Ulm, 89081, Germany
SOURCE: European Journal of Gastroenterology & Hepatology (2000), 12(1), 19-24
CODEN: EJGHES; ISSN: 0954-691X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background and aims: Low bone d. with an increased risk of vertebral fractures is a frequent complication in **inflammatory bowel disease**. Since the etiol. of osteopathia in these patients is different compared to postmenopausal or steroid-induced osteoporosis, no treatment strategy is established. Supplementation of calcium and vitamin D has been shown to prevent further bone loss, but no data are available showing the anabolic effect of sodium fluoride in Crohn's disease. Methods: We carried out a one-year prospective clin. trial in 33 patients with chronic active Crohn's disease who were randomly assigned to receive either calcium (500 mg b.i.d.) and 1000 IU **vitamin D3** only, or retarded-release sodium fluoride (25 mg t.i.d.) addnl. The diagnosis of Crohn's disease had been made at least two years ago, and all patients had received systemic high-dose steroid therapy during the previous year. Eleven of 15 patients who received calcium/vitamin D and 15 of 18 patients who addnl. received sodium fluoride completed the study. The primary endpoint of the study was the increase of bone mineral d., measured by dual energy x-ray absorptiometry (DXA) after one year of treatment. Bone-specific alk. phosphatase and osteocalcin were used as markers for bone turnover. Results: In the calcium/vitamin D only group, bone d. was not significantly changed after one year of treatment, whereas in the calcium/vitamin D/fluoride group, bone d. of the lumbar spine increased from -1.39.+-.0.3 (Z-score, mean .+-. SEM) to -0.65.+-.0.3 ($P<0.05$) after one year of treatment. Increase of bone d. was pos. correlated to the osteoblastic markers bone-specific alk. phosphatase ($r=0.53$) and osteocalcin ($r=0.43$). Conclusions: Sodium fluoride in combination with vitamin D and calcium is an effective, well-tolerated and inexpensive treatment to increase lumbar bone d. in patients with chronic active Crohn's disease and osteoporosis.
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

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FILE 'CAPLUS' ENTERED AT 12:10:26 ON 06 MAR 2003
L1 1 S EP0927721/PN
L2 20659 S VITAMIN D
L3 18 S L2 AND INFLAMMATORY BOWEL DISEASE
L4 8790 S VITAMIN D3
L5 4 S L4 AND INFLAMMATORY BOWEL DISEASE

=> d l3 1-18 ibib hitstr abs

L3 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:862660 CAPLUS
TITLE: Candidate Genes Colocalized to Linkage Regions in **Inflammatory Bowel Disease**
AUTHOR(S): Martin, K.; Radlmayr, M.; Borchers, R.; Heinzlmann, M.; Folwaczny, C.
CORPORATE SOURCE: Medizinische Klinik, Ludwig-Maximilians Universitaet Muenchen, Germany
SOURCE: Digestion (2002), 66(2), 121-126
CODEN: DIGEBW; ISSN: 0012-2823
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background and Aims: The genes encoding for tumor necrosis factor-.alpha. (TNF-.alpha.), epidermal growth factor receptor (EGFR) and the **vitamin D** receptor (VDR) are colocalized to **inflammatory bowel disease**-assocd. linkage regions on chromosomes 6, 7 and 12. An assocn. study of these gene polymorphisms with ulcerative colitis or Crohn's disease and a stratification according to disease phenotypes was performed in order to identify gentically homogenous subgroups. Patients and Methods: 119 healthy, unrelated controls, 95 patients with Crohn's disease and 93 patients with ulcerative colitis were genotyped for the (G to A) -308 TNF-.alpha. promoter polymorphism on chromosome 6, the codon 497 EGFR polymorphism on chromosome 7 and the TaqI polymorphism of the VDR gene on chromosome 12. After genotyping, patients were stratified according to the resp. disease phenotype. Results: A disequil. in the distribution of the VDR genotypes was found in patients with ulcerative colitis compared to controls ($p = 0.024$). In fistulizing and fibrostenotic Crohn's disease the TT' genotype was significantly reduced compared with other phenotypes ($p = 0.006$), whereas the tt' genotype was found more frequently ($p = 0.04$). The frequency of the WT allele of the EGFR gene was significantly higher in ulcerative colitis ($p = 0.04$) than in controls. Further significant differences, concerning the assocns. of the different polymorphisms and disease susceptibility or clin. phenotypes, were not obsd. Conclusions: Regardless of the disease phenotype, the assocns. between the polymorphisms and **inflammatory bowel disease** investigated herein are modest, even after stratification for the disease phenotypes. Hence, these polymorphisms are unlikely to confer the reported linkage between **inflammatory bowel disease** and chromosomes 6, 7 and 12.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:435941 CAPLUS
DOCUMENT NUMBER: 137:108032
TITLE: Interleukin-2 is one of the targets of 1,25-dihydroxyvitamin D3 in the immune system
AUTHOR(S): Bemiss, Candace J.; Mahon, Brett D.; Henry, Adam; Weaver, Veronika; Cantorna, Margherita T.
CORPORATE SOURCE: Department of Nutrition, The Pennsylvania State University, College of Health and Human Development, University Park, PA, 16802, USA
SOURCE: Archives of Biochemistry and Biophysics (2002), 402(2), 249-254
CODEN: ABBIA4; ISSN: 0003-9861
PUBLISHER: Elsevier Science

0034913

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Interleukin (IL)-2 knockout (KO) mice, which spontaneously develop symptoms of **inflammatory bowel disease** similar to ulcerative colitis in humans, were made **vitamin D** deficient (D-) or **vitamin D** sufficient (D+) or were supplemented with 1,25-dihydroxyvitamin D3 (1,25D3). 1,25-Dihydroxyvitamin D3 supplementation, but not **vitamin D** supplementation, reduced the early mortality of IL-2 KO mice. However, colitis severity was not different in D-, D+, or 1,25D3 IL-2 KO mice. Cells from D- IL-2 KO mice produced more interferon (IFN)-.gamma. than cells from all other mice. Con A-induced proliferation was upregulated in IL-2 KO mice and downregulated in wildtype (WT) mice fed 1,25D3. All other measured immune responses in cells from IL-2 KO mice were unchanged by **vitamin D** status. In vitro addn. of 1,25-dihydroxyvitamin D3 significantly reduced the prodn. of IL-10 and IFN-.gamma. in cells from D- and D+ WT mice. Conversely, IFN-.gamma. and IL-10 prodn. in cells from IL-2 KO mice were refractory to in vitro 1,25-dihydroxyvitamin D3 treatments. In the absence of IL-2, **vitamin D** was ineffective for suppressing colitis and ineffective for the in vitro downregulation of IL-10 or IFN-.gamma. prodn. One target of 1,25-dihydroxyvitamin D3 in the immune system is the IL-2 gene.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:425735 CAPLUS
DOCUMENT NUMBER: 137:41696
TITLE: Osteoporosis in **inflammatory bowel disease**: Effect of calcium and **vitamin D** with or without fluoride
AUTHOR(S): Abitbol, V.; Mary, J. Y.; Roux, C.; Soule, J. C.; Belaiche, J.; Dupas, J.-L.; Gendre, J. P.; Lerebours, E.; Chaussade, S.
CORPORATE SOURCE: The Groupe D'Etudes Therapeutiques Des Affections Inflammatoires Digestives (GETAID), Service de Gastroenterologie, Hopital Cochin, Paris, 75014, Fr.
SOURCE: Alimentary Pharmacology and Therapeutics (2002), 16(5), 919-927
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Previous data have indicated low bone formation as a mechanism of osteoporosis in **inflammatory bowel disease**. Fluoride can stimulate bone formation. The aim was to assess the effect of fluoride supplementation on lumbar spine bone mineral d. in osteoporotic patients with **inflammatory bowel disease** treated in parallel with calcium and **vitamin D**. In this prospective, randomized, double-blind, parallel and placebo-controlled study, 94 patients with **inflammatory bowel disease** (lumbar spine T score below - 2 std. deviations, normal serum 250H **vitamin D**), with a median age of 35 yr, were included. Bone mineral d. was measured by dual-energy X-ray absorptiometry. Patients were randomized to receive daily either sodium monofluorophosphate (150 mg, n = 45) or placebo (n = 49) for 1 yr, and all received calcium (1 g) and **vitamin D** (800 IU). The relative change in bone mineral d. from 0 to 12

mo was tested in each group (fluoride or placebo) and compared between the groups. Lumbar spine bone mineral d. increased significantly in both groups after 1 yr: 4.8 .+-. 5.6% (n = 29) and 3.2 .+-. 3.8% (n = 31) in the calcium-**vitamin D**-fluoride and calcium-**vitamin D**-placebo groups, resp. ($P < 0.001$ for each group). There was no difference between the groups ($P = 0.403$). Similar results were obsd. according to corticosteroid intake or disease activity. Calcium and **vitamin D** seem to increase lumbar spine d. in osteoporotic patients with **inflammatory bowel disease**: fluoride does not provide further benefit.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:217534 CAPLUS
DOCUMENT NUMBER: 137:107457
TITLE: **Vitamin D** status, parathyroid hormone and bone mineral density in patients with **inflammatory bowel disease**
AUTHOR(S): Jahnsen, J.; Falch, J. A.; Mowinckel, P.; Aadland, E.
CORPORATE SOURCE: Medical Dept. and Hormone Laboratory, Aker University Hospital, Oslo, NO-0514, Norway
SOURCE: Scandinavian Journal of Gastroenterology (2002), 37(2), 192-199
CODEN: SJGRA4; ISSN: 0036-5521
PUBLISHER: Taylor & Francis
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Although the pathogenesis of osteoporosis in **inflammatory bowel disease** (IBD) is not established, **vitamin D** deficiency and disturbances in calcium metab. are thought to be of importance, esp. in Crohn disease (CD). **Vitamin D** status is assessed and the relation between indexes of calcium metab., including 25-hydroxyvitamin D and parathyroid hormone concns., and bone mineral d. (BMD) in CD and ulcerative colitis (UC) are examd. 60 Patients with CD and 60 with UC were investigated. Each group comprised 24 men and 36 women. **Vitamin D** metabolites, parathyroid hormone and biochem. markers of bone metab. were measured in blood and urine. Lumbar spine, femoral neck and total body BMD were measured by dual x-ray absorptiometry (DXA) and Z-scores were obtained by comparison with age- and sex-matched normal values. Results: **Vitamin D** deficiency (25-hydroxyvitamin D3 <30 nmol/l) was present in 27% of patients with CD and in 15% with UC. Furthermore, CD patients had a significantly lower mean concn. of 25-hydroxyvitamin D3 compared with UC patients. **Vitamin D** status was not related to BMD at any of the skeletal sites measured. Secondary hyperparathyroidism was found in 10 out of 27 patients with CD after small-bowel resections. No differences were found in serum osteocalcin and urine pyridinoline between patients with CD and those with UC. Conclusions: Hypovitaminosis D is common in CD patients. Patients with CD and small-bowel resections are at risk of developing secondary hyperparathyroidism and low BMD.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:912535 CAPLUS
DOCUMENT NUMBER: 136:134027
TITLE: **Vitamin D**: its role and uses in immunology

0034913

AUTHOR(S): Deluca, Hector F.; Cantorna, Margherita T.
CORPORATE SOURCE: Department of Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706, USA
SOURCE: FASEB Journal (2001), 15(14), 2579-2585
CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review and discussion. In recent years there has been an effort to understand possible noncalcemic roles of **vitamin D**, including its role in the immune system and, in particular, on T cell-medicated immunity. **Vitamin D** receptor is found in significant concns. in the T lymphocyte and macrophage populations. However, its highest concn. is in the immature immune cells of the thymus and the mature CD-8 T lymphocytes. The significant role of **vitamin D** compds. as selective immunosuppressants is illustrated by their ability to either prevent or markedly suppress animal models of autoimmune disease. Results show that 1,25-dihydroxyvitamin D3 can either prevent or markedly suppress exptl. autoimmune encephalomyelitis, rheumatoid arthritis, systemic lupus erythematosus, type I diabetes, and **inflammatory bowel disease**. In almost every case, the action of the **vitamin D** hormone requires that the animals be maintained on a normal or high calcium diet. Possible mechanisms of suppression of these autoimmune disorders by the **vitamin D** hormone have been presented. The **vitamin D** hormone stimulates transforming growth factor TGF.beta.-1 and interleukin 4 (IL-4) prodn., which in turn may suppress inflammatory T cell activity. In support of this, the **vitamin D** hormone is unable to suppress a murine model of the human disease multiple sclerosis in IL-4-deficient mice. The results suggest an important role for **vitamin D** in autoimmune disorders and provide a fertile and interesting area of research that may yield important new therapies.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:472660 CAPLUS
DOCUMENT NUMBER: 135:56067
TITLE: Use of biologically active **vitamin D** compounds for the prevention and treatment of **inflammatory bowel disease**
INVENTOR(S): Hayes, Colleen E.; Nashold, Faye E.
PATENT ASSIGNEE(S): Northern Lights Pharmaceuticals, LLC, USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001046132	A1	20010628	WO 2000-US34913	20001221

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6358939	B1	20020319	US 1999-469985		19991221
EP 1240136	A1	20020918	EP 2000-986687		20001221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
US 2002128241	A1	20020912	US 2001-36819		20011221
NO 2002002974	A	20020820	NO 2002-2974		20020620
PRIORITY APPLN. INFO.:			US 1999-469985	A	19991221
			WO 2000-US34913	W	20001221

OTHER SOURCE(S): MARPAT 135:56067

AB Methods of treating **inflammatory bowel disease** are described, and in particular the prevention and treatment of **inflammatory bowel disease** in humans as well as other animals. These methods involve the administration of biol. active **vitamin D** compds., and therapeutic compns. thereof, so that the symptoms of **Inflammatory Bowel Disease** are reduced or relieved.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:435039 CAPLUS
DOCUMENT NUMBER: 135:41381
TITLE: Treatment of **inflammatory bowel disease** with **vitamin D** compounds
INVENTOR(S): Cantorna, Margherita T.
PATENT ASSIGNEE(S): The Penn State Research Foundation, USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001042205	A2	20010614	WO 2000-US42393	20001130
WO 2001042205	A3	20020321		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1233942	A2	20020828	EP 2000-992552	20001130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:			US 1999-168501P	P 19991202
			US 2000-197827P	P 20000414
			US 2000-208632P	P 20000601
			US 2000-231906P	P 20000911

WO 2000-US42393 W 20001130

OTHER SOURCE(S): MARPAT 135:41381

AB A method of treating **inflammatory bowel disease**, particularly ulcerative colitis and Crohn's disease, is disclosed. The method involves administering a **vitamin D** compd. in an amt. effective to treat the disease. The administration of a **vitamin D** compd. also prevents the development of or delays the onset of **inflammatory bowel disease** in susceptible individuals.

L3 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:255853 CAPLUS
DOCUMENT NUMBER: 134:271278
TITLE: Nutritional composition for treating inflammatory bowel diseases
INVENTOR(S): Snowden, Robert B.
PATENT ASSIGNEE(S): Snowden-Sutton Associates, Inc., USA
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6214373	B1	20010410	US 1999-414666	19991007
WO 2001024642	A1	20010412	WO 2000-US27404	20001005

W: CA
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1999-414666 A 19991007

AB A nutritional compn. and method useful for treatment of inflammatory bowel diseases is disclosed, the compn. comprising selected vitamins and mineral salts for oral administration to a subject having an **inflammatory bowel disease**. The compn. comprises an excess of **vitamin D** and vitamin B12 , contains vitamin C and iron in quantities promoting good absorption, contains water miscible forms of the fat-sol. vitamins, and no phosphate or carbonate salts. Preferably, the iron is present as ferrous fumarate. And, preferably the compn. is essentially free of magnesium. Preferred compn. consists of retinyl acetate 2,500, cholecalciferol 400, dl-.alpha.-tocopherol acetate 75 IU, phytonadione 40 .mu.g, ascorbic acid 100, thiamine mononitrate 5, riboflavin 5, pyridoxine hydrochloride 5 mg, cyanocobalamin 500 .mu.g, folic acid 0.2, niacinamide 10, biotin 0.15, pantothenic acid 5, iron 15, calcium 100, zinc 11.25 mg, selenium .mu.g, copper 1, manganese 1 mg, and iodine 75 .mu.g.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:787638 CAPLUS
DOCUMENT NUMBER: 134:41518
TITLE: 1,25-Dihydroxycholecalciferol prevents and ameliorates symptoms of experimental murine **inflammatory bowel disease**
AUTHOR(S): Cantorna, Margherita T.; Munsick, Carey; Bemiss, Candace; Mahon, Brett D.
CORPORATE SOURCE: Department of Nutrition, College of Health and Human

Development, Pennsylvania State University, University Park, PA, 16802, USA
SOURCE: Journal of Nutrition (2000), 130(11), 2648-2652
CODEN: JONUAI; ISSN: 0022-3166
PUBLISHER: American Society for Nutritional Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The amt. of **vitamin D** available from sunshine exposure or diet may be an important factor affecting the development of **inflammatory bowel disease** (IBD) in humans. We tested this hypothesis in an exptl. animal model of IBD. Interleukin (IL)-10 knockout (KO) mice, which spontaneously develop symptoms resembling human IBD, were made **vitamin D** deficient, **vitamin D** sufficient, or supplemented with active **vitamin D** (1,25-dihydroxycholecalciferol). The **vitamin D**-deficient mice rapidly developed diarrhea and wasting disease with mortality. The **vitamin D** -sufficient mice did not develop diarrhea, waste, or die. Supplementation with 50 IU cholecalciferol (5.0 .mu.g/day) or 1,25-dihydroxycholecalciferol (0.005 .mu.g/day) ameliorated the symptoms of IBD in mice. The 1,25-dihydroxycholecalciferol treatment (0.2 .mu.g/day) for as little as 2 wk blocked the progression and ameliorated the symptoms in mice with already established IBD.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:588387 CAPLUS
DOCUMENT NUMBER: 134:84446

TITLE: **Vitamin D** receptor gene polymorphism: association with Crohn's disease susceptibility

AUTHOR(S): Simmons, J. D.; Mullighan, C.; Welsh, K. I.; Jewell, D. P.
CORPORATE SOURCE: Gastroenterology Unit, Radcliffe Infirmary, University of Oxford, Oxford, OX2 6HE, UK

SOURCE: Gut (2000), 47(2), 211-214
CODEN: GUTTAK; ISSN: 0017-5749
PUBLISHER: BMJ Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The **vitamin D** receptor (VDR) gene represents a strong positional candidate susceptibility gene for **inflammatory bowel disease** (IBD). The VDR gene maps to a region on chromosome 12 that has been shown to be linked to IBD by genome screening techniques. It is the cellular receptor for 1,25(OH)2 vitamin D3 (calcitriol) which has a wide range of different regulatory effects on the immune system. IBD is characterized by activation of the mucosal immune system. The assocn. of polymorphisms in the VDR gene with susceptibility to IBD were studied. The subjects were European Caucasoids158 patients with ulcerative colitis, 245 with Crohn's disease, and 164 cadaveric renal allograft donor controls. Single nucleotide polymorphisms (TaqI, ApaI, and FokI) in VDR were typed in patients with Crohn's disease, ulcerative colitis, and controls by polymerase chain reaction with sequence specific primers. There were significantly more homozygotes for the TaqI polymorphism at codon 352 of exon 8 (genotype "tt") among patients with Crohn's disease (frequency 0.22) than patients with ulcerative colitis (0.12) or controls (0.12) (odds ratio 1.99; 95% confidence interval 1.14-3.47; p=0.017). This study provides preliminary evidence for a

genetic assocn. between Crohn's disease susceptibility and a gene that lies within one of the candidate regions detd. by linkage anal.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:246169 CAPLUS
DOCUMENT NUMBER: 132:260649
TITLE: Increase of bone mineral density with sodium fluoride in patients with Crohn's disease
AUTHOR(S): Von Tirpitz, Christian; Klaus, Jochen; Bruckel, Joachim; Rieber, Andrea; Scholer, Andre; Adler, Guido; Bohm, Bernhard O.; Reinshagen, Max
CORPORATE SOURCE: Department of Medicine, University of Ulm, Ulm, 89081, Germany
SOURCE: European Journal of Gastroenterology & Hepatology (2000), 12(1), 19-24
CODEN: EJGHES; ISSN: 0954-691X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background and aims: Low bone d. with an increased risk of vertebral fractures is a frequent complication in **inflammatory bowel disease**. Since the etiol. of osteopathia in these patients is different compared to postmenopausal or steroid-induced osteoporosis, no treatment strategy is established. Supplementation of calcium and **vitamin D** has been shown to prevent further bone loss, but no data are available showing the anabolic effect of sodium fluoride in Crohn's disease. Methods: We carried out a one-year prospective clin. trial in 33 patients with chronic active Crohn's disease who were randomly assigned to receive either calcium (500 mg b.i.d.) and 1000 IU vitamin D3 only, or retarded-release sodium fluoride (25 mg t.i.d.) addnl. The diagnosis of Crohn's disease had been made at least two years ago, and all patients had received systemic high-dose steroid therapy during the previous year. Eleven of 15 patients who received calcium/**vitamin D** and 15 of 18 patients who addnl. received sodium fluoride completed the study. The primary endpoint of the study was the increase of bone mineral d., measured by dual energy x-ray absorptiometry (DXA) after one year of treatment. Bone-specific alk. phosphatase and osteocalcin were used as markers for bone turnover. Results: In the calcium/**vitamin D** only group, bone d. was not significantly changed after one year of treatment, whereas in the calcium/**vitamin D**/fluoride group, bone d. of the lumbar spine increased from -1.39.+-.0.3 (Z-score, mean .+-. SEM) to -0.65.+-.0.3 ($P<0.05$) after one year of treatment. Increase of bone d. was pos. correlated to the osteoblastic markers bone-specific alk. phosphatase ($r=0.53$) and osteocalcin ($r=0.43$). Conclusions: Sodium fluoride in combination with **vitamin D** and calcium is an effective, well-tolerated and inexpensive treatment to increase lumbar bone d. in patients with chronic active Crohn's disease and osteoporosis.
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:242585 CAPLUS
DOCUMENT NUMBER: 132:264493
TITLE: Use of macro- and micronutrients for nutrition support in **inflammatory bowel disease**

0034913

AUTHOR(S): Alpers, David H.
CORPORATE SOURCE: Department of Medicine/Gastroenterology, Washington University School of Medicine, St. Louis, MO, USA
SOURCE: Nestle Nutrition Workshop Series, Clinical & Performance Programme (1999), 2(Inflammatory Bowel Diseases), 155-170
CODEN: NNWSFV; ISSN: 1422-7584
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 41 refs. followed by a discussion with 4 refs. This article reviews the need for and use of enteral and total parenteral nutrition in **inflammatory bowel disease** as adjunctive (not primary) treatment, and the provision of macronutrients parenterally at home. In addn., the recognition of deficiency states and use of cobalamin, iron, calcium and **vitamin D** are discussed.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:144772 CAPLUS
DOCUMENT NUMBER: 132:189689
TITLE: Bioreductive conjugates for drug targeting
INVENTOR(S): Adams, Ged; Blake, David; Naughton, Declan; Stratford, Ian
PATENT ASSIGNEE(S): Theramark Limited, UK; Adams, Margaret
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000010610	A2	20000302	WO 1999-GB2606	19990819
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9954296	A1	20000314	AU 1999-54296	19990819

PRIORITY APPLN. INFO.: GB 1998-18027 A 19980819
GB 1998-18156 A 19980820
WO 1999-GB2606 W 19990819
OTHER SOURCE(S): MARPAT 132:189689
AB The use of a bioreductive conjugate comprised of a noncytotoxic bioreductive moiety having linked thereto at least one therapeutic agent, and salts thereof, is disclosed for the healing of wounds and the treatment of fibrotic disorders, ulcerative colitis, **inflammatory bowel disease**, epilepsy, cardiovascular reperfusion injury, cerebral reperfusion injury, hypertension, cystic fibrosis, psoriasis, para-psoriasis, peptic ulcers, gastric ulcers, duodenal ulcers, diabetic ulcers dementia, oncol., AIDS, rheumatoid arthritis, diabetes, and ischemia. Various specific conjugates for treating these conditions

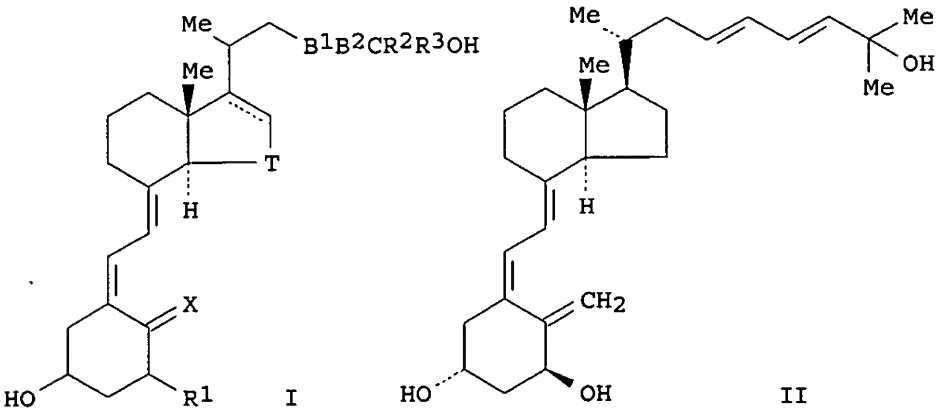
are also disclosed.

L3 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:77538 CAPLUS
DOCUMENT NUMBER: 130:139510
TITLE: Preparation of dihomo-seco-cholestanes with two unsaturated bonds in the side chain
INVENTOR(S): Barbier, Pierre; Mohr, Peter; Muller, Marc; Self, Christopher
PATENT ASSIGNEE(S): F.Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9903828	A1	19990128	WO 1998-EP4293	19980710
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9888602	A1	19990210	AU 1998-88602	19980710
EP 998455	A1	20000510	EP 1998-940201	19980710
R: DE, ES, FR, GB, IT				
JP 2001510183	T2	20010731	JP 2000-503057	19980710
US 5994569	A	19991130	US 1998-115188	19980714

PRIORITY APPLN. INFO.: EP 1997-112225 A 19970717
WO 1998-EP4293 W 19980710

OTHER SOURCE(S): MARPAT 130:139510
GI



AB Polyunsatd. 24a,24b-dihomo-9,10-secocholestane derivs. of formula I [B1, B2 = CH=CH, C.tplbond.C; T = CH2, CH2CH2; X = H2, CH2; R1 = H, F, OH; R2,

R3 = alkyl, CF3; CR2R3 = cycloalkyl] are prepd. and are useful in the treatment or prevention of **vitamin D** dependent disorders and of IL-12-dependent autoimmune diseases, particularly psoriasis, basal cell carcinomas, disorders of keratinization and keratosis, leukemia, osteoporosis, hyperparathyroidism accompanying renal failure, multiple sclerosis, transplant rejection, graft vs. host disease, rheumatoid arthritis, insulin-dependent diabetes mellitus, **inflammatory bowel disease**, septic shock and allergic encephalomyelitis. Thus, II was prepd. and was found to have an IC50 for the inhibition of IL-12 prodn. of 10 nM. Pharmaceutical compns. contg. I are described.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:640566 CAPLUS
DOCUMENT NUMBER: 127:268009
TITLE: Milk of transgenic animals containing human .alpha.1-antitrypsin and use of human .alpha.1-antitrypsin to treat bile acid-related diseases
INVENTOR(S): Carlson, Joyce; Janciauskiene, Sabina-Marija
PATENT ASSIGNEE(S): Carlson, Joyce, Swed.; Janciauskiene, Sabina-Marija
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9734628	A1	19970925	WO 1997-SE465	19970320
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
SE 9601091	A	19970922	SE 1996-1091	19960321
AU 9721864	A1	19971010	AU 1997-21864	19970320

PRIORITY APPLN. INFO.: SE 1996-1091 19960321
WO 1997-SE465 19970320

AB The use of human .alpha.1-antitrypsin as a foodstuff or as a medicament, utilizing its capacity to bind steroids and steroid-like substances, and transporting them in biol. systems is described. Particularly the direct oral administration of the milk of transgenic animals contg. abundant amts. (10-60 g/L) of human .alpha.1-AT to reinstate a defect in intestinal synthesis or to complement the normal physiol. biosynthesis of .alpha.1-AT is described. Such treatment will reduce the total body load of bile acids by increasing their gastrointestinal elimination. It is expected to be beneficial for bile acid-related diseases such as all cholestatic liver diseases, and bile-reflux gastritis. Such treatment is expected to be particularly beneficial in cases of neonatal cholestasis, as newborns circulate large quantities of hydrophobic bile acids which cause liver injury and may contribute to injury of other tissues. It will be protective in cases where bile acids cause tissue injury such as

vasculitis, glomerulonephritis, and **inflammatory bowel disease**. It will be beneficial against diarrhea, in intestinal bacterial overgrowth, and bile-acid malabsorption. Increased gastrointestinal elimination of the steroid structure may also reduce the total body load of cholesterol and thus be efficient in the treatment of hyperlipidemia.

L3 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:736027 CAPLUS
DOCUMENT NUMBER: 126:14824
TITLE: Corticosteroid-induced bone loss: Prevention and management
AUTHOR(S): Picado, Cesar; Luengo, Maite
CORPORATE SOURCE: Hospital Clinic i Universitari, Facultat de Medicina, Barcelona, Spain
SOURCE: Drug Safety (1996), 15(5), 347-359
CODEN: DRSAEA; ISSN: 0114-5916
PUBLISHER: Adis
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 125 refs. Osteoporosis is one of the most serious adverse effects experienced by patients receiving long term corticosteroid therapy. Bone loss occurs soon after corticosteroid therapy is initiated and results from a complex mechanism involving osteoblastic suppression and increased bone resorption. There are a no. of factors that may increase the risk of corticosteroid-induced osteoporosis [smoking, excessive alc. (ethanol) consumption, amenorrhea, relative immobilization, chronic obstructive pulmonary disease, **inflammatory bowel disease**, hypogonadism in men, organ transplantation]. The initial assessment of patients about to start taking corticosteroids should include measurement of spinal bone d., urinary calcium level and plasma calcifediol (25-hydroxycholecalciferol) level; serum testosterone levels should also be measured when hypogonadism is suspected. Many different drugs have been used to prevent osteoporosis in patients receiving long-term corticosteroid therapy, including thiazide diuretics, cholecalciferol (**vitamin D**) metabolites, bisphosphonates, calcitonin, fluoride, estrogens, anabolic steroids and progesterone. At present, however, published studies have failed to demonstrate a redn. in the rate of fracture using different preventive pharmacol. therapies in patients being treated with corticosteroids on a continuous basis. Among the drugs studied, bisphosphonates (pamidronic acid and etidronic acid) and calcitonin appear to be effective in increasing bone d. Cholecalciferol prepns. have been reported to be effective in some, but not all, studies. Limited data have shown pos. results with thiazide diuretics, estrogen, progesterone and nandrolone. When treating patients with corticosteroids, the lowest ED should be used, with topical corticosteroids used whenever possible. Auranofin may be considered in patients with corticosteroid-dependent asthma. Patients should take as much phys. activity as possible, maintain an adequate daily intake of calcium (1000 mg/day) and cholecalciferol (400 to 800 U/day), stop smoking and avoid excessive alc. intake. It is important to detect and treat hypogonadism in men, if present, and to replace gonadal hormones in postmenopausal women or amenorrheic premenopausal women, and to detect and correct cholecalciferol deficiency. A thiazide diuretic should be considered if hypercalciuria is present (urinary calcium excretion in excess of 4 mg/kg/day). High-risk patients and those with established osteoporosis should be treated with bisphosphonates (cyclical etidronic acid or i.v. pamidronic acid), nasal calcitonin, or calcifediol or calcitriol. Patients receiving cholecalciferol prepns. should be

carefully monitored for hypercalciuria and hypercalcemia.

L3 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:672001 CAPLUS
DOCUMENT NUMBER: 125:327076
TITLE: A randomized, placebo-controlled trial of calcium supplementation for decreased bone density in corticosteroid-using patients with **inflammatory bowel disease** : A pilot study
AUTHOR(S): Bernstein, C. N.; Seeger, L. L.; Anton, P. A.; Artinian, L.; Geffrey, S.; Goodman, W.; Belin, T. R.; Shanahan, F.
CORPORATE SOURCE: Departments Medicine, Radiology and Biostatistics, University Manitoba, Winnipeg, MB, R3A 1R9, Can.
SOURCE: Alimentary Pharmacology and Therapeutics (1996), 10(5), 777-786
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Patients with **inflammatory bowel disease** (IBD) have a high prevalence of osteoporosis. A no. of studies have found that corticosteroid use is assocd. with the development of osteoporosis in these patients. Calcium supplementation may be of benefit in corticosteroid-induced osteoporosis and calcium may be a nutrient that patients with IBD lack. The aim of this study was to test the benefit of calcium supplementation on bone d. in a pilot study over a 1-yr period, in a group of corticosteroid-using patients with IBD, in a randomized, double-blind, placebo-controlled treatment study. Corticosteroid-using patients with IBD including males over the age of 18 yr and premenopausal females, were randomized to receive either calcium carbonate 1000 mg plus **vitamin D** 250 IU (Oscal) or an identically matched placebo. Dual energy x-ray absorptiometry measurements of bone d. were obtained at entry and at 1 yr. At entry, and every 3 mo thereafter, serum was collected for the measurement of Hb, biochem. and bone hormones. Simultaneously a 24-h urine collection was analyzed for calcium excretion and creatinine clearance, and a 4-day food record was collected to document dietary calcium and **vitamin D** ingestion. The authors found a high prevalence of moderately severe decreased bone d. in corticosteroid-using patients with IBD. The dose of prednisone in the year prior to study entry was inversely correlated with bone d. at the hip ($R = -0.67$). At study entry serum osteocalcin was inversely correlated with corticosteroid dose in the year prior to the study ($R = -0.64$) and at study end, directly correlated with the percentage change in spine bone d. ($R = 0.59$). The dietary calcium intake of these patients was close to the current RDA (recommended daily intake) for premenopausal, post-adolescent adults. Calcium supplementation with small extra doses of **vitamin D** conferred no obvious benefit to bone d. at the end of 1 yr. There was no correlation between oral calcium ingestion and bone mass measurements. Both the treatment and placebo groups' bone d. remained relatively stable at 1 yr, suggesting that bone loss in corticosteroid-using patients may peak early into the use of the corticosteroids. Calcium supplementation (1000 mg/day) conferred no significant benefit to bone d. at 1 yr in patients with corticosteroid-using IBD patients with osteoporosis. Future investigations should explore other therapeutic avenues that may have greater effects on increasing bone d. in patients who already have considerable osteoporosis.

L3 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:311941 CAPLUS
DOCUMENT NUMBER: 122:78245
TITLE: Bone mineral density and calcium regulating hormones in patients with **inflammatory bowel disease** (Crohn's disease and ulcerative colitis)
AUTHOR(S): Sharla, S. H.; Minne, H. W.; Lempert, U. G.; Leidig, G.; Hauber, M.; Raedsch, R.; Ziegler, R.
CORPORATE SOURCE: Dep. Int. Med. IV, Univ. Heidelberg, Bad Pyrmont, Germany
SOURCE: Experimental and Clinical Endocrinology (1994), 102(1), 44-9
CODEN: EXCEDS; ISSN: 0232-7384
PUBLISHER: Barth
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Inflammatory bowel disease** (Crohn's disease and ulcerative colitis) is assocd. with decreased bone mineral d. and increased risk of osteoporosis. However, the pathogenesis of this bone loss is not yet fully understood. In the present study we measured lumbar bone mineral d. (by dual photon absorptiometry), serum levels of parathyroid hormone (PTH) and **vitamin D** metabolites, and serum markers of bone turnover (alk. phosphatase and osteocalcin) in 15 patients with Crohn's disease and in 4 patients with ulcerative colitis. The median duration of the disease was 4 yr and the median lifetime steroid dose was 10g of prednisone. We compared our results to a control group of 19 normal persons, who were matched for age and sex to the patients. We found that lumbar bone d. was reduced by 11% in patients compared with control persons (Z-score -0.6 .+-. 0.6 vs. -0.1 .+-. 0.8; $p<0.05$). In patients, the serum levels of PTH, 25-hydroxyvitamin D3, and calcitriol (1,25(OH)2D3) were significantly reduced compared with control persons. Serum alk. phosphatase activity (AP) was significantly higher in the patients and was inversely related to lumbar bone d. Osteocalcin values were not different between patients and control persons. There was also no difference in serum levels of calcium between the two groups, whereas phosphorus levels were higher in patients. We conclude that malabsorption of calcium was not a primary cause of bone loss in our patients, because we did not find secondary hyperparathyroidism. Accordingly, we did not find a severe **vitamin D** deficiency, since 25-hydroxyvitamin D3 levels were within the normal range. Therefore, our results favor the hypothesis that glucocorticoid therapy and/or the inflammatory process itself caused changes in bone metab. leading to a neg. bone balance with secondary redn. of PTH and calcitriol levels.

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(FILE 'HOME' ENTERED AT 12:10:14 ON 06 MAR 2003)

FILE 'CAPLUS' ENTERED AT 12:10:26 ON 06 MAR 2003
L1 1 S EP0927721/PN
L2 20659 S VITAMIN D
L3 18 S L2 AND INFLAMMATORY BOWEL DISEASE
L4 8790 S VITAMIN D3
L5 4 S L4 AND INFLAMMATORY BOWEL DISEASE

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NEWS 45   Feb 24  PCTGEN now available on STN
NEWS 46   Feb 24  TEMA now available on STN
NEWS 47   Feb 26  NTIS now allows simultaneous left and right truncation
NEWS 48   Feb 26  PCTFULL now contains images
NEWS 49   Mar 04  SDI PACKAGE for monthly delivery of multifile SDI results

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FILE LAST UPDATED: 5 Mar 2003 (20030305/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s ep0927721/pn
L1 1 EP0927721/PN
(EP927721/PN)

=> d l1 ibib hitstr abs

L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:404974 CAPLUS
DOCUMENT NUMBER: 131:59020
TITLE: Preparation of vitamin D derivatives with phosphorous atoms in the side chains
INVENTOR(S): Steinmeyer, Andreas; Neef, Gunter; Kirsch, Gerald; Schwarz, Katica; Wiesinger, Herbert; Haberey, Martin; Fahnrich, Marianne; Langer, Gernot
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9931112	A1	19990624	WO 1998-EP8137	19981216
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 927721	A1	19990707	EP 1997-250374	19971217 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
DE 19758119	C1	19990729	DE 1997-19758119	19971217
AU 9924134	A1	19990705	AU 1999-24134	19981216
EP 1042335	A1	20001011	EP 1998-966616	19981216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002508383	T2	20020319	JP 2000-539035	19981216

PRIORITY APPLN. INFO.:
DE 1997-19758119 A 19971217
EP 1997-250374 A 19971217
WO 1998-EP8137 W 19981216

OTHER SOURCE(S): MARPAT 131:59020
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

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AB The invention relates to novel vitamin D derivs. I [Y1 = H, OH, F, Cl, Br, O2CR5; Y2 = H, COR6; Y2O = .alpha.- or .beta.- bond; R1, R2 = H; R1R2 = CH2; R3, R4 = H, Cl, F, C1-4-alkyl; R3R4 = CH2; R3R4-C(20) = satd. or unsatd. C3-7-cycloalkyl; R5, R6 = C1-12-alkyl, aryl; VW = bond; V = W = OH; V = OH, W = H; X1, X2 = H, OH, OR7, O2CR7, PO(OR8)2, PO(NR82)2, PO(R8)2, OPO(OR8)2, OPO(NR82)2, OPO(R8)2, CH2PO(OR8)2, CH2PO(NR82)2, CH2PO(R8)2; R7 = C1-12-alkyl, aryl; R8 = H, C1-12-alkyl, aryl;; X1X2 = O; n = 0, 1; E1 = PO(OR9)2, PO(NR92)2, PO(R9)2, CO2R9; R9 = H, C1-12-alkyl, aryl; E2 = PO(OR9)2, PO(NR92)2, PO(R9)2, CO2R9, F, Cl, Br, H, C1-12-alkyl, aryl; Q = H, C1-12-alkyl, aryl, OH, O2CR10, F, Cl, Br, NH2, NHR10, N(R10)2; R10 = C1-12-alkyl, aryl; X1E2 = bond, X2 = H, OZ; Z = C1-12-alkyl, aryl, C1-12-acyl, aroyl, E2; X1X2E2Q = triple bond], a method for their prodn., intermediate products of the method as well as their use in producing medicaments. Thus, vitamin D analog II was prepd. from aldehyde III (TBDMS = SiMe2CMe3), via photochem. E/Z-isomerization, Horner-Emmons reaction with (MeO)2P(O)CH2CO2Me, condensation of unsatd. ester IV with MeP(O)(OMe)2 and desilylation with Dowex ion-exchange resin. II has an affinity for calcitriol receptors (competition factor = 10) and shows differentiation induction for HL-60 cells [DR50 = 22] and hypercalcemia induction [DR50 = >>100].

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=>
=> s vitamin D
      152450 VITAMIN
     1956515 D
L2     20659 VITAMIN D
             (VITAMIN(W)D)

=> s l2 and inflammatory bowel disease
      100292 INFLAMMATORY
        9855 BOWEL
      582905 DISEASE
        3110 INFLAMMATORY BOWEL DISEASE
             (INFLAMMATORY(W)BOWEL(W)DISEASE)
L3       18 L2 AND INFLAMMATORY BOWEL DISEASE

=> s vitamin D3
      152450 VITAMIN
       31725 D3
L4     8790 VITAMIN D3
             (VITAMIN(W)D3)

=> s l4 and inflammatory bowel disease
      100292 INFLAMMATORY
        9855 BOWEL
      582905 DISEASE
        3110 INFLAMMATORY BOWEL DISEASE
             (INFLAMMATORY(W)BOWEL(W)DISEASE)
L5        4 L4 AND INFLAMMATORY BOWEL DISEASE

=> d l5 ibib hitstr abs

L5   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:        2002:314727  CAPLUS
DOCUMENT NUMBER:         136:339498
```

0034913

TITLE: Methods for treating IL-18 mediated disorders
INVENTOR(S): Sims, John E.; Mohler, Kendall M.; Born, Teresa L.
PATENT ASSIGNEE(S): Immunex Corporation, USA
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032374	A2	20020425	WO 2001-US32460	20011017
WO 2002032374	A3	20020919		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002098185	A1	20020725	US 2002-981421	20020118

PRIORITY APPLN. INFO.: US 2000-241408P P 20001018
AB The invention pertains to methods for treating medical disorders characterized by elevated levels or abnormal expression of IL-18 by administering an IL-18 antagonist, such as sol. IL-18 receptor, a sol. IL-18 binding protein and/or an antibody.

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FILE 'CAPLUS' ENTERED AT 12:10:26 ON 06 MAR 2003
L1 1 S EP0927721/PN
L2 20659 S VITAMIN D
L3 18 S L2 AND INFLAMMATORY BOWEL DISEASE
L4 8790 S VITAMIN D3
L5 4 S L4 AND INFLAMMATORY BOWEL DISEASE

=> d l5 2-4 ibib hitstr abs

L5 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:147266 CAPLUS
DOCUMENT NUMBER: 134:364800
TITLE: Receptor polymorphisms and diseases
AUTHOR(S): Csaszar, A.; Abel, T.
CORPORATE SOURCE: Faculty of Health Sciences, Department of Medicine and Geriatrics, Semmelweis University, Budapest, H-1135, Hung.
SOURCE: European Journal of Pharmacology (2001), 414(1), 9-22
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with many refs. The aim of our review is to summarize common genetic variations of some receptors assocd. with clin. consequences,

which were not outlined in the previous special issue of this journal. Because of the multiple pathomechanisms of diseases, a set of genetic variation can play a role in the development of pathol. conditions. From the data available three articles would merit a greater interest. In systemic lupus erythematosus the assocns. related to some polymorphisms of Fc-, tumor necrosis factor (TNF) .alpha.- and interferon receptor may explore new autoimmunol. and inflammatory pathomechanisms. In the endocrinol., the androgen receptor repeat polymorphism will exert significant aspects in the development of prostate cancer. The pleiotropic responsibility of **vitamin D3** receptor polymorphism in the pathogenesis of immunol. disorders (primary biliary cirrhosis, **inflammatory bowel disease**, type 1 diabetes mellitus) and of malignancies (malignant melanoma, breast cancer) shed light on the importance of common nuclear receptors. Nevertheless, in the future studies a more consistent approach minimizing requirement bias in the selection of patients will approve our understanding the role of genetic influence on the pathogenesis of diseases.

REFERENCE COUNT: 84 THERE ARE 84 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:588387 CAPLUS
DOCUMENT NUMBER: 134:84446
TITLE: Vitamin D receptor gene polymorphism: association with Crohn's disease susceptibility
AUTHOR(S): Simmons, J. D.; Mullighan, C.; Welsh, K. I.; Jewell, D. P.
CORPORATE SOURCE: Gastroenterology Unit, Radcliffe Infirmary, University of Oxford, Oxford, OX2 6HE, UK
SOURCE: Gut (2000), 47(2), 211-214
CODEN: GUTTAK; ISSN: 0017-5749
PUBLISHER: BMJ Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The vitamin D receptor (VDR) gene represents a strong positional candidate susceptibility gene for **inflammatory bowel disease** (IBD). The VDR gene maps to a region on chromosome 12 that has been shown to be linked to IBD by genome screening techniques. It is the cellular receptor for 1,25(OH)2 **vitamin D3** (calcitriol) which has a wide range of different regulatory effects on the immune system. IBD is characterized by activation of the mucosal immune system. The assocn. of polymorphisms in the VDR gene with susceptibility to IBD were studied. The subjects were European Caucasoids158 patients with ulcerative colitis, 245 with Crohn's disease, and 164 cadaveric renal allograft donor controls. Single nucleotide polymorphisms (TaqI, ApaI, and FokI) in VDR were typed in patients with Crohn's disease, ulcerative colitis, and controls by polymerase chain reaction with sequence specific primers. There were significantly more homozygotes for the TaqI polymorphism at codon 352 of exon 8 (genotype "tt") among patients with Crohn's disease (frequency 0.22) than patients with ulcerative colitis (0.12) or controls (0.12) (odds ratio 1.99; 95% confidence interval 1.14-3.47; p=0.017). This study provides preliminary evidence for a genetic assocn. between Crohn's disease susceptibility and a gene that lies within one of the candidate regions detd. by linkage anal.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS

0034913

ACCESSION NUMBER: 2000:246169 CAPLUS
DOCUMENT NUMBER: 132:260649
TITLE: Increase of bone mineral density with sodium fluoride in patients with Crohn's disease
AUTHOR(S): Von Tirpitz, Christian; Klaus, Jochen; Bruckel, Joachim; Rieber, Andrea; Scholer, Andre; Adler, Guido; Bohm, Bernhard O.; Reinshagen, Max
CORPORATE SOURCE: Department of Medicine, University of Ulm, Ulm, 89081, Germany
SOURCE: European Journal of Gastroenterology & Hepatology (2000), 12(1), 19-24
CODEN: EJGHES; ISSN: 0954-691X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background and aims: Low bone d. with an increased risk of vertebral fractures is a frequent complication in **inflammatory bowel disease**. Since the etiol. of osteopathia in these patients is different compared to postmenopausal or steroid-induced osteoporosis, no treatment strategy is established. Supplementation of calcium and vitamin D has been shown to prevent further bone loss, but no data are available showing the anabolic effect of sodium fluoride in Crohn's disease. Methods: We carried out a one-year prospective clin. trial in 33 patients with chronic active Crohn's disease who were randomly assigned to receive either calcium (500 mg b.i.d.) and 1000 IU **vitamin D3** only, or retarded-release sodium fluoride (25 mg t.i.d.) addnl. The diagnosis of Crohn's disease had been made at least two years ago, and all patients had received systemic high-dose steroid therapy during the previous year. Eleven of 15 patients who received calcium/vitamin D and 15 of 18 patients who addnl. received sodium fluoride completed the study. The primary endpoint of the study was the increase of bone mineral d., measured by dual energy x-ray absorptiometry (DXA) after one year of treatment. Bone-specific alk. phosphatase and osteocalcin were used as markers for bone turnover. Results: In the calcium/vitamin D only group, bone d. was not significantly changed after one year of treatment, whereas in the calcium/vitamin D/fluoride group, bone d. of the lumbar spine increased from -1.39.+-.0.3 (Z-score, mean .+-. SEM) to -0.65.+-.0.3 ($P<0.05$) after one year of treatment. Increase of bone d. was pos. correlated to the osteoblastic markers bone-specific alk. phosphatase ($r=0.53$) and osteocalcin ($r=0.43$). Conclusions: Sodium fluoride in combination with vitamin D and calcium is an effective, well-tolerated and inexpensive treatment to increase lumbar bone d. in patients with chronic active Crohn's disease and osteoporosis.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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NEWS	3	Apr 09	BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS	4	Apr 09	ZDB will be removed from STN
NEWS	5	Apr 19	US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS	6	Apr 22	Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS	7	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS	8	Apr 22	Federal Research in Progress (FEDRIP) now available
NEWS	9	Jun 03	New e-mail delivery for search results now available
NEWS	10	Jun 10	MEDLINE Reload
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NEWS	12	Jul 02	FOREGE no longer contains STANDARDS file segment
NEWS	13	Jul 22	USAN to be reloaded July 28, 2002; saved answer sets no longer valid
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NEWS	16	Aug 08	CANCERLIT reload
NEWS	17	Aug 08	PHARMAMarketLetter(PHARMAML) - new on STN
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NEWS	22	Aug 26	Sequence searching in REGISTRY enhanced
NEWS	23	Sep 03	JAPIO has been reloaded and enhanced
NEWS	24	Sep 16	Experimental properties added to the REGISTRY file
NEWS	25	Sep 16	CA Section Thesaurus available in CAPLUS and CA
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NEWS	27	Oct 21	EVENTLINE has been reloaded
NEWS	28	Oct 24	BEILSTEIN adds new search fields
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NEWS	31	Nov 18	DKILIT has been renamed APOLLIT
NEWS	32	Nov 25	More calculated properties added to REGISTRY
NEWS	33	Dec 02	TIBKAT will be removed from STN
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NEWS	35	Dec 17	PCTFULL now covers WP/PCT Applications from 1978 to date
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NEWS	41	Jan 21	PHARMAML offering one free connect hour in February 2003
NEWS	42	Jan 29	Simultaneous left and right truncation added to COMPENDEX, ENERGY, INSPEC
NEWS	43	Feb 13	CANCERLIT is no longer being updated

0034913

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NEWS 44   Feb 24  METADEX enhancements
NEWS 45   Feb 24  PCTGEN now available on STN
NEWS 46   Feb 24  TEMA now available on STN
NEWS 47   Feb 26  NTIS now allows simultaneous left and right truncation
NEWS 48   Feb 26  PCTFULL now contains images
NEWS 49   Mar 04  SDI PACKAGE for monthly delivery of multifile SDI results

NEWS EXPRESS  January 6 CURRENT WINDOWS VERSION IS V6.01a,
              CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
              AND CURRENT DISCOVER FILE IS DATED 01 OCTOBER 2002
NEWS HOURS    STN Operating Hours Plus Help Desk Availability
NEWS INTER    General Internet Information
NEWS LOGIN    Welcome Banner and News Items
NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
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                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

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0034913

FILE COVERS 1907 - 6 Mar 2003 VOL 138 ISS 10
FILE LAST UPDATED: 5 Mar 2003 (20030305/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s ep0927721/pn
L1 1 EP0927721/PN
(EP927721/PN)

=> d l1 ibib hitstr abs

L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:404974 CAPLUS
DOCUMENT NUMBER: 131:59020
TITLE: Preparation of vitamin D derivatives with phosphorous atoms in the side chains
INVENTOR(S): Steinmeyer, Andreas; Neef, Gunter; Kirsch, Gerald; Schwarz, Katica; Wiesinger, Herbert; Haberey, Martin; Fahnrich, Marianne; Langer, Gernot
PATENT ASSIGNEE(S): Schering A.-G., Germany
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9931112	A1	19990624	WO 1998-EP8137	19981216
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 927721	A1	19990707	EP 1997-250374	19971217 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
DE 19758119	C1	19990729	DE 1997-19758119	19971217
AU 9924134	A1	19990705	AU 1999-24134	19981216
EP 1042335	A1	20001011	EP 1998-966616	19981216
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002508383	T2	20020319	JP 2000-539035	19981216

PRIORITY APPLN. INFO.: DE 1997-19758119 A 19971217
EP 1997-250374 A 19971217
WO 1998-EP8137 W 19981216
OTHER SOURCE(S): MARPAT 131:59020
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The invention relates to novel vitamin D derivs. I [Y1 = H, OH, F, Cl, Br, O2CR5; Y2 = H, COR6; Y2O = .alpha.- or .beta.- bond; R1, R2 = H; R1R2 = CH2; R3, R4 = H, Cl, F, C1-4-alkyl; R3R4 = CH2; R3R4-C(20) = satd. or unsatd. C3-7-cycloalkyl; R5, R6 = C1-12-alkyl, aryl; VW = bond; V = W = OH; V = OH, W = H; X1, X2 = H, OH, OR7, O2CR7, PO(OR8)2, PO(NR82)2, PO(R8)2, OPO(OR8)2, OPO(NR82)2, OPO(R8)2, CH2PO(OR8)2, CH2PO(NR82)2, CH2PO(R8)2; R7 = C1-12-alkyl, aryl; R8 = H, C1-12-alkyl, aryl;; X1X2 = O; n = 0, 1; E1 = PO(OR9)2, PO(NR92)2, PO(R9)2, CO2R9; R9 = H, C1-12-alkyl, aryl; E2 = PO(OR9)2, PO(NR92)2, PO(R9)2, CO2R9, F, Cl, Br, H, C1-12-alkyl, aryl; Q = H, C1-12-alkyl, aryl, OH, O2CR10, F, Cl, Br, NH2, NHR10, N(R10)2; R10 = C1-12-alkyl, aryl; X1E2 = bond, X2 = H, OZ; Z = C1-12-alkyl, aryl, C1-12-acyl, aroyl, E2; X1X2E2Q = triple bond], a method for their prodn., intermediate products of the method as well as their use in producing medicaments. Thus, vitamin D analog II was prepd. from aldehyde III (TBDMS = SiMe2CMe3), via photochem. E/Z-isomerization, Horner-Emmons reaction with (MeO)2P(O)CH2CO2Me, condensation of unsatd. ester IV with MeP(O)(OMe)2 and desilylation with Dowex ion-exchange resin. II has an affinity for calcitriol receptors (competition factor = 10) and shows differentiation induction for HL-60 cells [DR50 = 22] and hypercalcemia induction [DR50 = >>100].

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=>
=> s vitamin D
        152450 VITAMIN
       1956515 D
L2       20659 VITAMIN D
                 (VITAMIN(W)D)

=> s l2 and inflammatory bowel disease
        100292 INFLAMMATORY
          9855 BOWEL
        582905 DISEASE
          3110 INFLAMMATORY BOWEL DISEASE
                 (INFLAMMATORY(W)BOWEL(W)DISEASE)
L3          18 L2 AND INFLAMMATORY BOWEL DISEASE

=> s vitamin D3
        152450 VITAMIN
         31725 D3
L4        8790 VITAMIN D3
                 (VITAMIN(W)D3)

=> s l4 and inflammatory bowel disease
        100292 INFLAMMATORY
          9855 BOWEL
        582905 DISEASE
          3110 INFLAMMATORY BOWEL DISEASE
                 (INFLAMMATORY(W)BOWEL(W)DISEASE)
L5           4 L4 AND INFLAMMATORY BOWEL DISEASE

=> d l5 ibib hitstr abs

L5   ANSWER 1 OF 4  CAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:        2002:314727  CAPLUS
DOCUMENT NUMBER:         136:339498
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0034913

TITLE: Methods for treating IL-18 mediated disorders
INVENTOR(S): Sims, John E.; Mohler, Kendall M.; Born, Teresa L.
PATENT ASSIGNEE(S): Immunex Corporation, USA
SOURCE: PCT Int. Appl., 53 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002032374	A2	20020425	WO 2001-US32460	20011017
WO 2002032374	A3	20020919		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002098185	A1	20020725	US 2002-981421	20020118

PRIORITY APPLN. INFO.: US 2000-241408P P 20001018

AB The invention pertains to methods for treating medical disorders characterized by elevated levels or abnormal expression of IL-18 by administering an IL-18 antagonist, such as sol. IL-18 receptor, a sol. IL-18 binding protein and/or an antibody.

=> d his

(FILE 'HOME' ENTERED AT 12:10:14 ON 06 MAR 2003)

FILE 'CAPLUS' ENTERED AT 12:10:26 ON 06 MAR 2003

L1 1 S EP0927721/PN
L2 20659 S VITAMIN D
L3 18 S L2 AND INFLAMMATORY BOWEL DISEASE
L4 8790 S VITAMIN D3
L5 4 S L4 AND INFLAMMATORY BOWEL DISEASE

=> d l5 2-4 ibib hitstr abs

L5 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:147266 CAPLUS
DOCUMENT NUMBER: 134:364800
TITLE: Receptor polymorphisms and diseases
AUTHOR(S): Csaszar, A.; Abel, T.
CORPORATE SOURCE: Faculty of Health Sciences, Department of Medicine and Geriatrics, Semmelweis University, Budapest, H-1135, Hung.
SOURCE: European Journal of Pharmacology (2001), 414(1), 9-22
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with many refs. The aim of our review is to summarize common genetic variations of some receptors assocd. with clin. consequences,

which were not outlined in the previous special issue of this journal. Because of the multiple pathomechanisms of diseases, a set of genetic variation can play a role in the development of pathol. conditions. From the data available three articles would merit a greater interest. In systemic lupus erythematosus the assocns. related to some polymorphisms of Fc-, tumor necrosis factor (TNF) .alpha.- and interferon receptor may explore new autoimmunol. and inflammatory pathomechanisms. In the endocrinol., the androgen receptor repeat polymorphism will exert significant aspects in the development of prostate cancer. The pleiotropic responsibility of **vitamin D3** receptor polymorphism in the pathogenesis of immunol. disorders (primary biliary cirrhosis, **inflammatory bowel disease**, type 1 diabetes mellitus) and of malignancies (malignant melanoma, breast cancer) shed light on the importance of common nuclear receptors. Nevertheless, in the future studies a more consistent approach minimizing requirement bias in the selection of patients will approve our understanding the role of genetic influence on the pathogenesis of diseases.

REFERENCE COUNT: 84 THERE ARE 84 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:588387 CAPLUS
DOCUMENT NUMBER: 134:84446
TITLE: Vitamin D receptor gene polymorphism: association with Crohn's disease susceptibility
AUTHOR(S): Simmons, J. D.; Mullighan, C.; Welsh, K. I.; Jewell, D. P.
CORPORATE SOURCE: Gastroenterology Unit, Radcliffe Infirmary, University of Oxford, Oxford, OX2 6HE, UK
SOURCE: Gut (2000), 47(2), 211-214
CODEN: GUTTAK; ISSN: 0017-5749
PUBLISHER: BMJ Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The vitamin D receptor (VDR) gene represents a strong positional candidate susceptibility gene for **inflammatory bowel disease** (IBD). The VDR gene maps to a region on chromosome 12 that has been shown to be linked to IBD by genome screening techniques. It is the cellular receptor for 1,25(OH)2 **vitamin D3** (calcitriol) which has a wide range of different regulatory effects on the immune system. IBD is characterized by activation of the mucosal immune system. The assocn. of polymorphisms in the VDR gene with susceptibility to IBD were studied. The subjects were European Caucasoids158 patients with ulcerative colitis, 245 with Crohn's disease, and 164 cadaveric renal allograft donor controls. Single nucleotide polymorphisms (TaqI, ApaI, and FokI) in VDR were typed in patients with Crohn's disease, ulcerative colitis, and controls by polymerase chain reaction with sequence specific primers. There were significantly more homozygotes for the TaqI polymorphism at codon 352 of exon 8 (genotype "tt") among patients with Crohn's disease (frequency 0.22) than patients with ulcerative colitis (0.12) or controls (0.12) (odds ratio 1.99; 95% confidence interval 1.14-3.47; p=0.017). This study provides preliminary evidence for a genetic assocn. between Crohn's disease susceptibility and a gene that lies within one of the candidate regions detd. by linkage anal.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2003 ACS

0034913

ACCESSION NUMBER: 2000:246169 CAPLUS
DOCUMENT NUMBER: 132:260649
TITLE: Increase of bone mineral density with sodium fluoride in patients with Crohn's disease
AUTHOR(S): Von Tirpitz, Christian; Klaus, Jochen; Bruckel, Joachim; Rieber, Andrea; Scholer, Andre; Adler, Guido; Bohm, Bernhard O.; Reinshagen, Max
CORPORATE SOURCE: Department of Medicine, University of Ulm, Ulm, 89081, Germany
SOURCE: European Journal of Gastroenterology & Hepatology (2000), 12(1), 19-24
CODEN: EJGHES; ISSN: 0954-691X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background and aims: Low bone d. with an increased risk of vertebral fractures is a frequent complication in **inflammatory bowel disease**. Since the etiol. of osteopathia in these patients is different compared to postmenopausal or steroid-induced osteoporosis, no treatment strategy is established. Supplementation of calcium and vitamin D has been shown to prevent further bone loss, but no data are available showing the anabolic effect of sodium fluoride in Crohn's disease. Methods: We carried out a one-year prospective clin. trial in 33 patients with chronic active Crohn's disease who were randomly assigned to receive either calcium (500 mg b.i.d.) and 1000 IU **vitamin D3** only, or retarded-release sodium fluoride (25 mg t.i.d.) addnl. The diagnosis of Crohn's disease had been made at least two years ago, and all patients had received systemic high-dose steroid therapy during the previous year. Eleven of 15 patients who received calcium/vitamin D and 15 of 18 patients who addnl. received sodium fluoride completed the study. The primary endpoint of the study was the increase of bone mineral d., measured by dual energy x-ray absorptiometry (DXA) after one year of treatment. Bone-specific alk. phosphatase and osteocalcin were used as markers for bone turnover. Results: In the calcium/vitamin D only group, bone d. was not significantly changed after one year of treatment, whereas in the calcium/vitamin D/fluoride group, bone d. of the lumbar spine increased from -1.39.+-.0.3 (Z-score, mean .+-. SEM) to -0.65.+-.0.3 ($P<0.05$) after one year of treatment. Increase of bone d. was pos. correlated to the osteoblastic markers bone-specific alk. phosphatase ($r=0.53$) and osteocalcin ($r=0.43$). Conclusions: Sodium fluoride in combination with vitamin D and calcium is an effective, well-tolerated and inexpensive treatment to increase lumbar bone d. in patients with chronic active Crohn's disease and osteoporosis.
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 12:10:14 ON 06 MAR 2003)

FILE 'CAPLUS' ENTERED AT 12:10:26 ON 06 MAR 2003
L1 1 S EP0927721/PN
L2 20659 S VITAMIN D
L3 18 S L2 AND INFLAMMATORY BOWEL DISEASE
L4 8790 S VITAMIN D3
L5 4 S L4 AND INFLAMMATORY BOWEL DISEASE

=> d l3 1-18 ibib hitstr abs

L3 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:862660 CAPLUS
TITLE: Candidate Genes Colocalized to Linkage Regions in **Inflammatory Bowel Disease**
AUTHOR(S): Martin, K.; Radlmayr, M.; Borchers, R.; Heinzlmann, M.; Folwaczny, C.
CORPORATE SOURCE: Medizinische Klinik, Ludwig-Maximilians Universitaet Muenchen, Germany
SOURCE: Digestion (2002), 66(2), 121-126
CODEN: DIGEBW; ISSN: 0012-2823
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background and Aims: The genes encoding for tumor necrosis factor-.alpha. (TNF-.alpha.), epidermal growth factor receptor (EGFR) and the **vitamin D** receptor (VDR) are colocalized to **inflammatory bowel disease**-assocd. linkage regions on chromosomes 6, 7 and 12. An assocn. study of these gene polymorphisms with ulcerative colitis or Crohn's disease and a stratification according to disease phenotypes was performed in order to identify gentically homogenous subgroups. Patients and Methods: 119 healthy, unrelated controls, 95 patients with Crohn's disease and 93 patients with ulcerative colitis were genotyped for the (G to A) -308 TNF-.alpha. promoter polymorphism on chromosome 6, the codon 497 EGFR polymorphism on chromosome 7 and the TaqI polymorphism of the VDR gene on chromosome 12. After genotyping, patients were stratified according to the resp. disease phenotype. Results: A disequil. in the distribution of the VDR genotypes was found in patients with ulcerative colitis compared to controls ($p = 0.024$). In fistulizing and fibrostenotic Crohn's disease the TT' genotype was significantly reduced compared with other phenotypes ($p = 0.006$), whereas the tt' genotype was found more frequently ($p = 0.04$). The frequency of the WT allele of the EGFR gene was significantly higher in ulcerative colitis ($p = 0.04$) than in controls. Further significant differences, concerning the assocns. of the different polymorphisms and disease susceptibility or clin. phenotypes, were not obsd. Conclusions: Regardless of the disease phenotype, the assocns. between the polymorphisms and **inflammatory bowel disease** investigated herein are modest, even after stratification for the disease phenotypes. Hence, these polymorphisms are unlikely to confer the reported linkage between **inflammatory bowel disease** and chromosomes 6, 7 and 12.
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:435941 CAPLUS
DOCUMENT NUMBER: 137:108032
TITLE: Interleukin-2 is one of the targets of 1,25-dihydroxyvitamin D3 in the immune system
AUTHOR(S): Bemiss, Candace J.; Mahon, Brett D.; Henry, Adam; Weaver, Veronika; Cantorna, Margherita T.
CORPORATE SOURCE: Department of Nutrition, The Pennsylvania State University, College of Health and Human Development, University Park, PA, 16802, USA
SOURCE: Archives of Biochemistry and Biophysics (2002), 402(2), 249-254
CODEN: ABBIA4; ISSN: 0003-9861
PUBLISHER: Elsevier Science

0034913

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Interleukin (IL)-2 knockout (KO) mice, which spontaneously develop symptoms of **inflammatory bowel disease** similar to ulcerative colitis in humans, were made **vitamin D** deficient (D-) or **vitamin D** sufficient (D+) or were supplemented with 1,25-dihydroxyvitamin D3 (1,25D3). 1,25-Dihydroxyvitamin D3 supplementation, but not **vitamin D** supplementation, reduced the early mortality of IL-2 KO mice. However, colitis severity was not different in D-, D+, or 1,25D3 IL-2 KO mice. Cells from D- IL-2 KO mice produced more interferon (IFN)-.gamma. than cells from all other mice. Con A-induced proliferation was upregulated in IL-2 KO mice and downregulated in wildtype (WT) mice fed 1;25D3. All other measured immune responses in cells from IL-2 KO mice were unchanged by **vitamin D** status. In vitro addn. of 1,25-dihydroxyvitamin D3 significantly reduced the prodn. of IL-10 and IFN-.gamma. in cells from D- and D+ WT mice. Conversely, IFN-.gamma. and IL-10 prodn: in cells from IL-2 KO mice were refractory to in vitro 1,25-dihydroxyvitamin D3 treatments. In the absence of IL-2, **vitamin D** was ineffective for suppressing colitis and ineffective for the in vitro downregulation of IL-10 or IFN-.gamma. prodn. One target of 1,25-dihydroxyvitamin D3 in the immune system is the IL-2 gene.
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:425735 CAPLUS
DOCUMENT NUMBER: 137:41696
TITLE: Osteoporosis in **inflammatory bowel disease**: Effect of calcium and **vitamin D** with or without fluoride
AUTHOR(S): Abitbol, V.; Mary, J. Y.; Roux, C.; Soule, J. C.; Belaiche, J.; Dupas, J.-L.; Gendre, J. P.; Lerebours, E.; Chaussade, S.
CORPORATE SOURCE: The Groupe D'Etudes Therapeutiques Des Affections Inflammatoires Digestives (GETAID), Service de Gastroenterologie, Hopital Cochin, Paris, 75014, Fr.
SOURCE: Alimentary Pharmacology and Therapeutics (2002), 16(5), 919-927
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Previous data have indicated low bone formation as a mechanism of osteoporosis in **inflammatory bowel disease**. Fluoride can stimulate bone formation. The aim was to assess the effect of fluoride supplementation on lumbar spine bone mineral d. in osteoporotic patients with **inflammatory bowel disease** treated in parallel with calcium and **vitamin D**. In this prospective, randomized, double-blind, parallel and placebo-controlled study, 94 patients with **inflammatory bowel disease** (lumbar spine T score below - 2 std. deviations, normal serum 250H **vitamin D**), with a median age of 35 yr, were included. Bone mineral d. was measured by dual-energy X-ray absorptiometry. Patients were randomized to receive daily either sodium monofluorophosphate (150 mg, n = 45) or placebo (n = 49) for 1 yr, and all received calcium (1 g) and **vitamin D** (800 IU). The relative change in bone mineral d. from 0 to 12

mo was tested in each group (fluoride or placebo) and compared between the groups. Lumbar spine bone mineral d. increased significantly in both groups after 1 yr: 4.8 .+-. 5.6% (n = 29) and 3.2 .+-. 3.8% (n = 31) in the calcium-**vitamin D**-fluoride and calcium-**vitamin D**-placebo groups, resp. (P < 0.001 for each group). There was no difference between the groups (P = 0.403). Similar results were obsd. according to corticosteroid intake or disease activity. Calcium and **vitamin D** seem to increase lumbar spine d. in osteoporotic patients with **inflammatory bowel disease**: fluoride does not provide further benefit.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:217534 CAPLUS
DOCUMENT NUMBER: 137:107457
TITLE: **Vitamin D** status, parathyroid hormone and bone mineral density in patients with **inflammatory bowel disease**
AUTHOR(S): Jahnsen, J.; Falch, J. A.; Mowinckel, P.; Aadland, E.
CORPORATE SOURCE: Medical Dept. and Hormone Laboratory, Aker University Hospital, Oslo, NO-0514, Norway
SOURCE: Scandinavian Journal of Gastroenterology (2002), 37(2), 192-199
CODEN: SJGRA4; ISSN: 0036-5521
PUBLISHER: Taylor & Francis
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Although the pathogenesis of osteoporosis in **inflammatory bowel disease** (IBD) is not established, **vitamin D** deficiency and disturbances in calcium metab. are thought to be of importance, esp. in Crohn disease (CD). **Vitamin D** status is assessed and the relation between indexes of calcium metab., including 25-hydroxyvitamin D and parathyroid hormone concns., and bone mineral d. (BMD) in CD and ulcerative colitis (UC) are examd. 60 Patients with CD and 60 with UC were investigated. Each group comprised 24 men and 36 women. **Vitamin D** metabolites, parathyroid hormone and biochem. markers of bone metab. were measured in blood and urine. Lumbar spine, femoral neck and total body BMD were measured by dual x-ray absorptiometry (DXA) and Z-scores were obtained by comparison with age- and sex-matched normal values. Results: **Vitamin D** deficiency (25-hydroxyvitamin D3 <30 nmol/l) was present in 27% of patients with CD and in 15% with UC. Furthermore, CD patients had a significantly lower mean concn. of 25-hydroxyvitamin D3 compared with UC patients. **Vitamin D** status was not related to BMD at any of the skeletal sites measured. Secondary hyperparathyroidism was found in 10 out of 27 patients with CD after small-bowel resections. No differences were found in serum osteocalcin and urine pyridinoline between patients with CD and those with UC. Conclusions: Hypovitaminosis D is common in CD patients. Patients with CD and small-bowel resections are at risk of developing secondary hyperparathyroidism and low BMD.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:912535 CAPLUS
DOCUMENT NUMBER: 136:134027
TITLE: **Vitamin D**: its role and uses in immunology

AUTHOR(S): Deluca, Hector F.; Cantorna, Margherita T.
CORPORATE SOURCE: Department of Biochemistry, University of Wisconsin-Madison, Madison, WI, 53706, USA
SOURCE: FASEB Journal (2001), 15(14), 2579-2585
CODEN: FAJOEC; ISSN: 0892-6638
PUBLISHER: Federation of American Societies for Experimental Biology
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review and discussion. In recent years there has been an effort to understand possible noncalcemic roles of **vitamin D**, including its role in the immune system and, in particular, on T cell-medicated immunity. **Vitamin D** receptor is found in significant concns. in the T lymphocyte and macrophage populations. However, its highest concn. is in the immature immune cells of the thymus and the mature CD-8 T lymphocytes. The significant role of **vitamin D** compds. as selective immunosuppressants is illustrated by their ability to either prevent or markedly suppress animal models of autoimmune disease. Results show that 1,25-dihydroxyvitamin D3 can either prevent or markedly suppress exptl. autoimmune encephalomyelitis, rheumatoid arthritis, systemic lupus erythematosus, type I diabetes, and **inflammatory bowel disease**. In almost every case, the action of the **vitamin D** hormone requires that the animals be maintained on a normal or high calcium diet. Possible mechanisms of suppression of these autoimmune disorders by the **vitamin D** hormone have been presented. The **vitamin D** hormone stimulates transforming growth factor TGF.beta.-1 and interleukin 4 (IL-4) prodn., which in turn may suppress inflammatory T cell activity. In support of this, the **vitamin D** hormone is unable to suppress a murine model of the human disease multiple sclerosis in IL-4-deficient mice. The results suggest an important role for **vitamin D** in autoimmune disorders and provide a fertile and interesting area of research that may yield important new therapies.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:472660 CAPLUS
DOCUMENT NUMBER: 135:56067
TITLE: Use of biologically active **vitamin D** compounds for the prevention and treatment of **inflammatory bowel disease**
INVENTOR(S): Hayes, Colleen E.; Nashold, Faye E.
PATENT ASSIGNEE(S): Northern Lights Pharmaceuticals, LLC, USA
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001046132	A1	20010628	WO 2000-US34913	20001221

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6358939	B1	20020319	US 1999-469985	19991221
EP 1240136	A1	20020918	EP 2000-986687	20001221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2002128241	A1	20020912	US 2001-36819	20011221
NO 2002002974	A	20020820	NO 2002-2974	20020620
PRIORITY APPLN. INFO.:			US 1999-469985 A	19991221
			WO 2000-US34913 W	20001221

OTHER SOURCE(S): MARPAT 135:56067

AB Methods of treating **inflammatory bowel disease** are described, and in particular the prevention and treatment of **inflammatory bowel disease** in humans as well as other animals. These methods involve the administration of biol. active **vitamin D** compds., and therapeutic compns. thereof, so that the symptoms of **Inflammatory Bowel Disease** are reduced or relieved.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:435039 CAPLUS
DOCUMENT NUMBER: 135:41381
TITLE: Treatment of **inflammatory bowel disease** with **vitamin D** compounds
INVENTOR(S): Cantorna, Margherita T.
PATENT ASSIGNEE(S): The Penn State Research Foundation, USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001042205	A2	20010614	WO 2000-US42393	20001130
WO 2001042205	A3	20020321		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1233942	A2	20020828	EP 2000-992552	20001130
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
PRIORITY APPLN. INFO.:			US 1999-168501P P	19991202
			US 2000-197827P P	20000414
			US 2000-208632P P	20000601
			US 2000-231906P P	20000911

US 10/148,620

WO 2000-US42393 W 20001130

OTHER SOURCE(S): MARPAT 135:41381

AB A method of treating **inflammatory bowel disease**, particularly ulcerative colitis and Crohn's disease, is disclosed. The method involves administering a **vitamin D** compd. in an amt. effective to treat the disease. The administration of a **vitamin D** compd. also prevents the development of or delays the onset of **inflammatory bowel disease** in susceptible individuals.

L3 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:255853 CAPLUS
DOCUMENT NUMBER: 134:271278
TITLE: Nutritional composition for treating inflammatory bowel diseases
INVENTOR(S): Snowden, Robert B.
PATENT ASSIGNEE(S): Snowden-Sutton Associates, Inc., USA
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6214373	B1	20010410	US 1999-414666	19991007
WO 2001024642	A1	20010412	WO 2000-US27404	20001005

W: CA
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1999-414666 A 19991007

AB A nutritional compn. and method useful for treatment of inflammatory bowel diseases is disclosed, the compn. comprising selected vitamins and mineral salts for oral administration to a subject having an **inflammatory bowel disease**. The compn. comprises an excess of **vitamin D** and vitamin B12 , contains vitamin C and iron in quantities promoting good absorption, contains water miscible forms of the fat-sol. vitamins, and no phosphate or carbonate salts. Preferably, the iron is present as ferrous fumarate. And, preferably the compn. is essentially free of magnesium. Preferred compn. consists of retinyl acetate 2,500, cholecalciferol 400, dl-.alpha.-tocopherol acetate 75 IU, phytonadione 40 .mu.g, ascorbic acid 100, thiamine mononitrate 5, riboflavin 5, pyridoxine hydrochloride 5 mg, cyanocobalamin 500 .mu.g, folic acid 0.2, niacinamide 10, biotin 0.15, pantothenic acid 5, iron 15, calcium 100, zinc 11.25 mg, selenium .mu.g, copper 1, manganese 1 mg, and iodine 75 .mu.g.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:787638 CAPLUS
DOCUMENT NUMBER: 134:41518
TITLE: 1,25-Dihydroxycholecalciferol prevents and ameliorates symptoms of experimental murine **inflammatory bowel disease**
AUTHOR(S): Cantorna, Margherita T.; Munsick, Carey; Bemiss, Candace; Mahon, Brett D.
CORPORATE SOURCE: Department of Nutrition, College of Health and Human

0034913

Development, Pennsylvania State University, University Park, PA, 16802, USA
SOURCE: Journal of Nutrition (2000), 130(11), 2648-2652
CODEN: JONUAI; ISSN: 0022-3166
PUBLISHER: American Society for Nutritional Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The amt. of **vitamin D** available from sunshine exposure or diet may be an important factor affecting the development of **inflammatory bowel disease** (IBD) in humans. We tested this hypothesis in an exptl. animal model of IBD. Interleukin (IL)-10 knockout (KO) mice, which spontaneously develop symptoms resembling human IBD, were made **vitamin D** deficient, **vitamin D** sufficient, or supplemented with active **vitamin D** (1,25-dihydroxycholecalciferol). The **vitamin D**-deficient mice rapidly developed diarrhea and wasting disease with mortality. The **vitamin D** -sufficient mice did not develop diarrhea, waste, or die. Supplementation with 50 IU cholecalciferol (5.0 .mu.g/day) or 1,25-dihydroxycholecalciferol (0.005 .mu.g/day) ameliorated the symptoms of IBD in mice. The 1,25-dihydroxycholecalciferol treatment (0.2 .mu.g/day) for as little as 2 wk blocked the progression and ameliorated the symptoms in mice with already established IBD.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:588387 CAPLUS
DOCUMENT NUMBER: 134:84446
TITLE: **Vitamin D** receptor gene polymorphism: association with Crohn's disease susceptibility
AUTHOR(S): Simmons, J. D.; Mullighan, C.; Welsh, K. I.; Jewell, D. P.
CORPORATE SOURCE: Gastroenterology Unit, Radcliffe Infirmary, University of Oxford, Oxford, OX2 6HE, UK
SOURCE: Gut (2000), 47(2), 211-214
CODEN: GUTTAK; ISSN: 0017-5749
PUBLISHER: BMJ Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The **vitamin D** receptor (VDR) gene represents a strong positional candidate susceptibility gene for **inflammatory bowel disease** (IBD). The VDR gene maps to a region on chromosome 12 that has been shown to be linked to IBD by genome screening techniques. It is the cellular receptor for 1,25(OH)2 vitamin D3 (calcitriol) which has a wide range of different regulatory effects on the immune system. IBD is characterized by activation of the mucosal immune system. The assocn. of polymorphisms in the VDR gene with susceptibility to IBD were studied. The subjects were European Caucasoids158 patients with ulcerative colitis, 245 with Crohn's disease, and 164 cadaveric renal allograft donor controls. Single nucleotide polymorphisms (TaqI, ApaI, and FokI) in VDR were typed in patients with Crohn's disease, ulcerative colitis, and controls by polymerase chain reaction with sequence specific primers. There were significantly more homozygotes for the TaqI polymorphism at codon 352 of exon 8 (genotype "tt") among patients with Crohn's disease (frequency 0.22) than patients with ulcerative colitis (0.12) or controls (0.12) (odds ratio 1.99; 95% confidence interval 1.14-3.47; p=0.017). This study provides preliminary evidence for a

genetic assocn. between Crohn's disease susceptibility and a gene that lies within one of the candidate regions detd. by linkage anal.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:246169 CAPLUS
DOCUMENT NUMBER: 132:260649
TITLE: Increase of bone mineral density with sodium fluoride in patients with Crohn's disease
AUTHOR(S): Von Tirpitz, Christian; Klaus, Jochen; Bruckel, Joachim; Rieber, Andrea; Scholer, Andre; Adler, Guido; Bohm, Bernhard O.; Reinshagen, Max
CORPORATE SOURCE: Department of Medicine, University of Ulm, Ulm, 89081, Germany
SOURCE: European Journal of Gastroenterology & Hepatology (2000), 12(1), 19-24
CODEN: EJGHES; ISSN: 0954-691X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background and aims: Low bone d. with an increased risk of vertebral fractures is a frequent complication in **inflammatory bowel disease**. Since the etiol. of osteopathia in these patients is different compared to postmenopausal or steroid-induced osteoporosis, no treatment strategy is established. Supplementation of calcium and **vitamin D** has been shown to prevent further bone loss, but no data are available showing the anabolic effect of sodium fluoride in Crohn's disease. Methods: We carried out a one-year prospective clin. trial in 33 patients with chronic active Crohn's disease who were randomly assigned to receive either calcium (500 mg b.i.d.) and 1000 IU vitamin D3 only, or retarded-release sodium fluoride (25 mg t.i.d.) addnl. The diagnosis of Crohn's disease had been made at least two years ago, and all patients had received systemic high-dose steroid therapy during the previous year. Eleven of 15 patients who received calcium/**vitamin D** and 15 of 18 patients who addnl. received sodium fluoride completed the study. The primary endpoint of the study was the increase of bone mineral d., measured by dual energy x-ray absorptiometry (DXA) after one year of treatment. Bone-specific alk. phosphatase and osteocalcin were used as markers for bone turnover. Results: In the calcium/**vitamin D** only group, bone d. was not significantly changed after one year of treatment, whereas in the calcium/**vitamin D**/fluoride group, bone d. of the lumbar spine increased from -1.39.+-.0.3 (Z-score, mean .+-. SEM) to -0.65.+-.0.3 ($P<0.05$) after one year of treatment. Increase of bone d. was pos. correlated to the osteoblastic markers bone-specific alk. phosphatase ($r=0.53$) and osteocalcin ($r=0.43$). Conclusions: Sodium fluoride in combination with **vitamin D** and calcium is an effective, well-tolerated and inexpensive treatment to increase lumbar bone d. in patients with chronic active Crohn's disease and osteoporosis.
REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:242585 CAPLUS
DOCUMENT NUMBER: 132:264493
TITLE: Use of macro- and micronutrients for nutrition support in **inflammatory bowel disease**

0034913

AUTHOR(S): Alpers, David H.
CORPORATE SOURCE: Department of Medicine/Gastroenterology, Washington University School of Medicine, St. Louis, MO, USA
SOURCE: Nestle Nutrition Workshop Series, Clinical & Performance Programme (1999), 2(Inflammatory Bowel Diseases), 155-170
CODEN: NNWSFV; ISSN: 1422-7584
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 41 refs. followed by a discussion with 4 refs. This article reviews the need for and use of enteral and total parenteral nutrition in **inflammatory bowel disease** as adjunctive (not primary) treatment, and the provision of macronutrients parenterally at home. In addn., the recognition of deficiency states and use of cobalamin, iron, calcium and **vitamin D** are discussed.
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:144772 CAPLUS
DOCUMENT NUMBER: 132:189689
TITLE: Bioreductive conjugates for drug targeting
INVENTOR(S): Adams, Ged; Blake, David; Naughton, Declan; Stratford, Ian
PATENT ASSIGNEE(S): Theramark Limited, UK; Adams, Margaret
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000010610	A2	20000302	WO 1999-GB2606	19990819
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9954296	A1	20000314	AU 1999-54296	19990819

PRIORITY APPLN. INFO.: GB 1998-18027 A 19980819
GB 1998-18156 A 19980820
WO 1999-GB2606 W 19990819
OTHER SOURCE(S): MARPAT 132:189689
AB The use of a bioreductive conjugate comprised of a noncytotoxic bioreductive moiety having linked thereto at least one therapeutic agent, and salts thereof, is disclosed for the healing of wounds and the treatment of fibrotic disorders, ulcerative colitis, **inflammatory bowel disease**, epilepsy, cardiovascular reperfusion injury, cerebral reperfusion injury, hypertension, cystic fibrosis, psoriasis, para-psoriasis, peptic ulcers, gastric ulcers, duodenal ulcers, diabetic ulcers dementia, oncol., AIDS, rheumatoid arthritis, diabetes, and ischemia. Various specific conjugates for treating these conditions

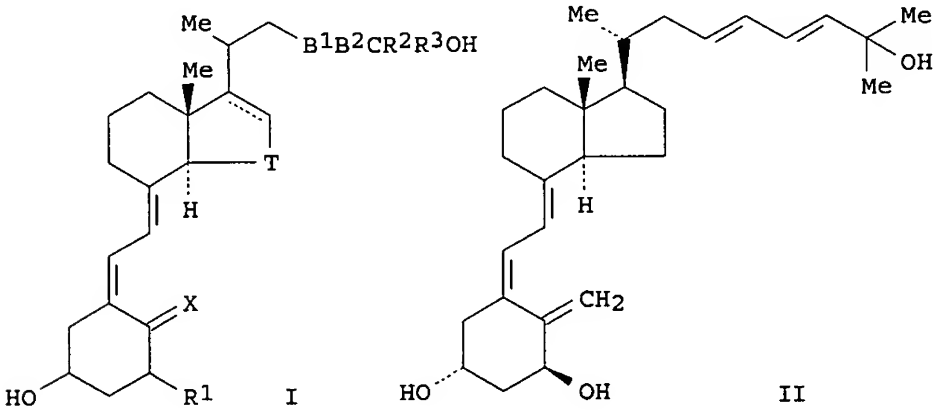
are also disclosed.

L3 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:77538 CAPLUS
DOCUMENT NUMBER: 130:139510
TITLE: Preparation of dihomo-seco-cholestanes with two unsaturated bonds in the side chain
INVENTOR(S): Barbier, Pierre; Mohr, Peter; Muller, Marc; Self, Christopher
PATENT ASSIGNEE(S): F.Hoffmann-La Roche A.-G., Switz.
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9903828	A1	19990128	WO 1998-EP4293	19980710
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9888602	A1	19990210	AU 1998-88602	19980710
EP 998455	A1	20000510	EP 1998-940201	19980710
R: DE, ES, FR, GB, IT				
JP 2001510183	T2	20010731	JP 2000-503057	19980710
US 5994569	A	19991130	US 1998-115188	19980714

PRIORITY APPLN. INFO.: EP 1997-112225 A 19970717
WO 1998-EP4293 W 19980710

OTHER SOURCE(S): MARPAT 130:139510
GI



AB Polyunsatd. 24a,24b-dihomo-9,10-secocholestane derivs. of formula I [B1, B2 = CH=CH, C.tplbond.C; T = CH2, CH2CH2; X = H2, CH2; R1 = H, F, OH; R2,

R3 = alkyl, CF3; CR2R3 = cycloalkyl] are prepd. and are useful in the treatment or prevention of **vitamin D** dependent disorders and of IL-12-dependent autoimmune diseases, particularly psoriasis, basal cell carcinomas, disorders of keratinization and keratosis, leukemia, osteoporosis, hyperparathyroidism accompanying renal failure, multiple sclerosis, transplant rejection, graft vs. host disease, rheumatoid arthritis, insulin-dependent diabetes mellitus, **inflammatory bowel disease**, septic shock and allergic encephalomyelitis. Thus, II was prepd. and was found to have an IC50 for the inhibition of IL-12 prodn. of 10 nM. Pharmaceutical compns. contg. I are described.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:640566 CAPLUS
DOCUMENT NUMBER: 127:268009
TITLE: Milk of transgenic animals containing human .alpha.1-antitrypsin and use of human .alpha.1-antitrypsin to treat bile acid-related diseases
INVENTOR(S): Carlson, Joyce; Janciauskiene, Sabina-Marija
PATENT ASSIGNEE(S): Carlson, Joyce, Swed.; Janciauskiene, Sabina-Marija
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9734628	A1	19970925	WO 1997-SE465	19970320
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
SE 9601091	A	19970922	SE 1996-1091	19960321
AU 9721864	A1	19971010	AU 1997-21864	19970320

PRIORITY APPLN. INFO.: SE 1996-1091 19960321
WO 1997-SE465 19970320

AB The use of human .alpha.1-antitrypsin as a foodstuff or as a medicament, utilizing its capacity to bind steroids and steroid-like substances, and transporting them in biol. systems is described. Particularly the direct oral administration of the milk of transgenic animals contg. abundant amts. (10-60 g/L) of human .alpha.1-AT to reinstate a defect in intestinal synthesis or to complement the normal physiol. biosynthesis of .alpha.1-AT is described. Such treatment will reduce the total body load of bile acids by increasing their gastrointestinal elimination. It is expected to be beneficial for bile acid-related diseases such as all cholestatic liver diseases, and bile-reflux gastritis. Such treatment is expected to be particularly beneficial in cases of neonatal cholestasis, as newborns circulate large quantities of hydrophobic bile acids which cause liver injury and may contribute to injury of other tissues. It will be protective in cases where bile acids cause tissue injury such as

vasculitis, glomerulonephritis, and **inflammatory bowel disease**. It will be beneficial against diarrhea, in intestinal bacterial overgrowth, and bile-acid malabsorption. Increased gastrointestinal elimination of the steroid structure may also reduce the total body load of cholesterol and thus be efficient in the treatment of hyperlipidemia.

L3 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:736027 CAPLUS
DOCUMENT NUMBER: 126:14824
TITLE: Corticosteroid-induced bone loss: Prevention and management
AUTHOR(S): Picado, Cesar; Luengo, Maite
CORPORATE SOURCE: Hospital Clinic i Universitari, Facultat de Medicina, Barcelona, Spain
SOURCE: Drug Safety (1996), 15(5), 347-359
CODEN: DRSAEA; ISSN: 0114-5916
PUBLISHER: Adis
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 125 refs. Osteoporosis is one of the most serious adverse effects experienced by patients receiving long term corticosteroid therapy. Bone loss occurs soon after corticosteroid therapy is initiated and results from a complex mechanism involving osteoblastic suppression and increased bone resorption. There are a no. of factors that may increase the risk of corticosteroid-induced osteoporosis [smoking, excessive alc. (ethanol) consumption, amenorrhea, relative immobilization, chronic obstructive pulmonary disease, **inflammatory bowel disease**, hypogonadism in men, organ transplantation]. The initial assessment of patients about to start taking corticosteroids should include measurement of spinal bone d., urinary calcium level and plasma calcifediol (25-hydroxycholecalciferol) level; serum testosterone levels should also be measured when hypogonadism is suspected. Many different drugs have been used to prevent osteoporosis in patients receiving long-term corticosteroid therapy, including thiazide diuretics, cholecalciferol (**vitamin D**) metabolites, bisphosphonates, calcitonin, fluoride, estrogens, anabolic steroids and progesterone. At present, however, published studies have failed to demonstrate a redn. in the rate of fracture using different preventive pharmacol. therapies in patients being treated with corticosteroids on a continuous basis. Among the drugs studied, bisphosphonates (pamidronic acid and etidronic acid) and calcitonin appear to be effective in increasing bone d. Cholecalciferol prepns. have been reported to be effective in some, but not all, studies. Limited data have shown pos. results with thiazide diuretics, estrogen, progesterone and nandrolone. When treating patients with corticosteroids, the lowest ED should be used, with topical corticosteroids used whenever possible. Auranofin may be considered in patients with corticosteroid-dependent asthma. Patients should take as much phys. activity as possible, maintain an adequate daily intake of calcium (1000 mg/day) and cholecalciferol (400 to 800 U/day), stop smoking and avoid excessive alc. intake. It is important to detect and treat hypogonadism in men, if present, and to replace gonadal hormones in postmenopausal women or amenorrheic premenopausal women, and to detect and correct cholecalciferol deficiency. A thiazide diuretic should be considered if hypercalciuria is present (urinary calcium excretion in excess of 4 mg/kg/day). High-risk patients and those with established osteoporosis should be treated with bisphosphonates (cyclical etidronic acid or i.v. pamidronic acid), nasal calcitonin, or calcifediol or calcitriol. Patients receiving cholecalciferol prepns. should be

carefully monitored for hypercalciuria and hypercalcemia.

L3 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:672001 CAPLUS
DOCUMENT NUMBER: 125:327076
TITLE: A randomized, placebo-controlled trial of calcium supplementation for decreased bone density in corticosteroid-using patients with **inflammatory bowel disease** : A pilot study
AUTHOR(S): Bernstein, C. N.; Seeger, L. L.; Anton, P. A.; Artinian, L.; Geffrey, S.; Goodman, W.; Belin, T. R.; Shanahan, F.
CORPORATE SOURCE: Departments Medicine, Radiology and Biostatistics, University Manitoba, Winnipeg, MB, R3A 1R9, Can.
SOURCE: Alimentary Pharmacology and Therapeutics (1996), 10(5), 777-786
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Patients with **inflammatory bowel disease** (IBD) have a high prevalence of osteoporosis. A no. of studies have found that corticosteroid use is assocd. with the development of osteoporosis in these patients. Calcium supplementation may be of benefit in corticosteroid-induced osteoporosis and calcium may be a nutrient that patients with IBD lack. The aim of this study was to test the benefit of calcium supplementation on bone d. in a pilot study over a 1-yr period, in a group of corticosteroid-using patients with IBD, in a randomized, double-blind, placebo-controlled treatment study. Corticosteroid-using patients with IBD including males over the age of 18 yr and premenopausal females, were randomized to receive either calcium carbonate 1000 mg plus **vitamin D** 250 IU (Oscal) or an identically matched placebo. Dual energy x-ray absorptiometry measurements of bone d. were obtained at entry and at 1 yr. At entry, and every 3 mo thereafter, serum was collected for the measurement of Hb, biochem. and bone hormones. Simultaneously a 24-h urine collection was analyzed for calcium excretion and creatinine clearance, and a 4-day food record was collected to document dietary calcium and **vitamin D** ingestion. The authors found a high prevalence of moderately severe decreased bone d. in corticosteroid-using patients with IBD. The dose of prednisone in the year prior to study entry was inversely correlated with bone d. at the hip ($R = -0.67$). At study entry serum osteocalcin was inversely correlated with corticosteroid dose in the year prior to the study ($R = -0.64$) and at study end, directly correlated with the percentage change in spine bone d. ($R = 0.59$). The dietary calcium intake of these patients was close to the current RDA (recommended daily intake) for premenopausal, post-adolescent adults. Calcium supplementation with small extra doses of **vitamin D** conferred no obvious benefit to bone d. at the end of 1 yr. There was no correlation between oral calcium ingestion and bone mass measurements. Both the treatment and placebo groups' bone d. remained relatively stable at 1 yr, suggesting that bone loss in corticosteroid-using patients may peak early into the use of the corticosteroids. Calcium supplementation (1000 mg/day) conferred no significant benefit to bone d. at 1 yr in patients with corticosteroid-using IBD patients with osteoporosis. Future investigations should explore other therapeutic avenues that may have greater effects on increasing bone d. in patients who already have considerable osteoporosis.

0034913

L3 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:311941 CAPLUS
DOCUMENT NUMBER: 122:78245
TITLE: Bone mineral density and calcium regulating hormones in patients with **inflammatory bowel disease** (Crohn's disease and ulcerative colitis)
AUTHOR(S): Sharla, S. H.; Minne, H. W.; Lempert, U. G.; Leidig, G.; Hauber, M.; Raedsch, R.; Ziegler, R.
CORPORATE SOURCE: Dep. Int. Med. IV, Univ. Heidelberg, Bad Pyrmont, Germany
SOURCE: Experimental and Clinical Endocrinology (1994), 102(1), 44-9
CODEN: EXCEDS; ISSN: 0232-7384
PUBLISHER: Barth
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Inflammatory bowel disease** (Crohn's disease and ulcerative colitis) is assocd. with decreased bone mineral d. and increased risk of osteoporosis. However, the pathogenesis of this bone loss is not yet fully understood. In the present study we measured lumbar bone mineral d. (by dual photon absorptiometry), serum levels of parathyroid hormone (PTH) and **vitamin D** metabolites, and serum markers of bone turnover (alk. phosphatase and osteocalcin) in 15 patients with Crohn's disease and in 4 patients with ulcerative colitis. The median duration of the disease was 4 yr and the median lifetime steroid dose was 10g of prednisone. We compared our results to a control group of 19 normal persons, who were matched for age and sex to the patients. We found that lumbar bone d. was reduced by 11% in patients compared with control persons (Z-score -0.6 .+-. 0.6 vs. -0.1 .+-. 0.8; $p<0.05$). In patients, the serum levels of PTH, 25-hydroxyvitamin D3, and calcitriol (1,25(OH)2D3) were significantly reduced compared with control persons. Serum alk. phosphatase activity (AP) was significantly higher in the patients and was inversely related to lumbar bone d. Osteocalcin values were not different between patients and control persons. There was also no difference in serum levels of calcium between the two groups, whereas phosphorus levels were higher in patients. We conclude that malabsorption of calcium was not a primary cause of bone loss in our patients, because we did not find secondary hyperparathyroidism. Accordingly, we did not find a severe **vitamin D** deficiency, since 25-hydroxyvitamin D3 levels were within the normal range. Therefore, our results favor the hypothesis that glucocorticoid therapy and/or the inflammatory process itself caused changes in bone metab. leading to a neg. bone balance with secondary redn. of PTH and calcitriol levels.